Filed on behalf of: Accord BioPharma, Inc.
By: Lora M. Green (lgreen@geminilaw.com)

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ACCORD BIOPHARMA, INC., INTAS PHARMACEUTICALS LTD., AND BIO-THERA SOLUTIONS, LTD.,
Petitioner,

v.

JANSSEN BIOTECH, INC.,
Patent Owner.

Case No. IPR2026-00256
Patent No. 11,014,982

PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 11,014,982

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I. INTRODUCTION

Accord BioPharma, Inc., Intas Pharmaceuticals Ltd., and Bio-Thera Solutions, Ltd. ("Petitioner" or "Accord") respectfully requests *inter partes* review of claims 1-10 of US11,014,982 ("*US982,*" EX1002), assigned to Janssen Biotech, Inc. ("Janssen" or "PO").

The claims are directed to a method of treating active ankylosing spondylitis ("AS") in which an antibody having heavy chain and light chain sequences found in golimumab is administered intravenously ("IV") at a dose of 2 mg/kg at weeks 0 and 4, then every 8 weeks thereafter. This method is anticipated by a clinical trial sponsored by Janssen, NCT02186873 ("*NCT873-V24*") (EX1014), which disclosed the exact same IV dose and schedule for the treatment of active AS. *NCT873-V24* was publicly available more than one year prior to the earliest possible effective filing date of *US982* and is prior art.

The claims issued only because Janssen failed to disclose *NCT873-V24* to the examiner, leading the examiner to erroneously conclude that the prior art did not teach administering golimumab to AS patients intravenously. Had Janssen directed the examiner's attention to *NCT873-V24*—its own prior art—the examiner would have gleaned that it disclosed not only IV administration to AS patients, but all the other steps of the claimed method, and *US982* never would have issued.

While the challenged claims also recite specific efficacy parameters the claimed method of treatment must achieve, these parameters merely describe the results Janssen obtained when it treated AS patients with the method disclosed in *NCT873-V24*. The parameters do not alter or modify the steps of the method and thus cannot distinguish it over Janssen's disclosure of the method in *NCT873-V24*. Moreover, the law is clear that an obvious method cannot be made non-obvious merely by claiming the results it produces. *Baxter Healthcare Corp. v. Millenium Biologix, LLC*, IPR2013-00590, Paper 49 at 7–8 (PTAB Mar. 18, 2015) (claim elements were not entitled to patentable weight because they "list various intended results," "do not recite positive acts that are carried out as part of the claimed methods," and do not "specify any limitation on the manner in which the [method] step is to be carried out"); *id.* at 10-11; *Fresenius-Kabi USA LLC v. Cubist Pharms., Inc.*, Case No. IPR2015-00227, Paper 13 at 5–7 (PTAB May 14, 2015) (holding that "the requirement of 'minimiz[ing] skeletal muscle toxicity' would be understood as nothing more than the intended result or consequence of administering daptomycin at the specifically recited dosage interval" because it "does not require anything beyond administering daptomycin at the express dosage intervals recited in the claims").

While Janssen will no doubt attempt to save its obvious claims by alleging that the method produced better-than-expected efficacy, as it did during

prosecution, this is not supported by the law or facts. At best for Janssen, the small alleged improvement in efficacy is a difference in degree, not kind. Such a difference is entitled to little weight as secondary evidence of non-obviousness. *In re Huang,* 100 F.3d 135, 139 (Fed. Cir. 1996) (even modifications to the prior art that result in "great improvement and utility" are not patentable unless they "produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art").

Further, Janssen cannot marshal evidence sufficient to prove the claimed method produces improved efficacy over prior art golimumab treatments, *e.g.*, Janssen's subcutaneous golimumab treatment for AS, because it did not conduct a head-to-head clinical trial. Such a trial would have been necessary to substantiate Janssen's allegation.

Finally, a person of ordinary skill in the art ("POSA") would have expected the claimed method to be very effective for treating AS. Long before the earliest possible effective filing date of *US982*, it was well known that a cytokine (messaging protein) known as TNFα played a key role in the molecular etiology of RA, AS, and psoriatic arthritis ("PsA"), which are closely related diseases characterized by chronic inflammation and the damage that accrues therefrom. Because of this common mechanism, TNFα inhibitors such as golimumab were known to be equally effective at treating all three

diseases. Indeed, in 2009, long before the earliest possible effective filing date of *US982*, the U.S. Food & Drug Administration ("FDA") had approved Janssen's subcutaneous golimumab product, marketed as SIMPONI, as an effective treatment for all three diseases. Moreover, *the same dose and dosing schedule were approved as effective for all three diseases*. In 2013, FDA also approved Janssen's SIMPONI ARIA golimumab product, a follow-on IV formulation of golimumab, as effective for treating RA, and Janssen was also testing the same dose and dosing schedule for PsA.

Crucially, the approved dose of SIMPONI ARIA was 2 mg/kg of golimumab infused over 30 minutes at weeks 0 and 4, then every 8 weeks thereafter, *which is identical to the method of the challenged claims*. Janssen published that this dose and schedule were the product of pharmacokinetic modeling intended to produce sustained plasma levels that met or exceeded those produced by SIMPONI. Given the equivalent efficacy of SC and IV golimumab for RA, the efficacy of SC golimumab for PsA, and the data showing that the IV dose produced the same or higher serum levels as the SC dose, a POSA would have had far more than a reasonable expectation that SIMPONI ARIA would be very effective for AS. Indeed, as explained in the accompanying declaration of Dr. Roy Fleischmann, a prominent rheumatologist with many decades of experience researching and prescribing golimumab and other TNFα inhibitors to

treat RA, AS, and PsA, the skilled practitioner would only have been surprised if the claimed dosing regimen failed to effectively treat AS.

US982 should be seen for what it is: the invalid fruit of Janssen's scheme to hide key prior art from the examiner to evergreen its patent protection for SIMPONI ARIA and frustrate competition by lower-cost biosimilar products. PTAB review is necessary to prevent the public from having to pay higher prices because of Janssen's gaming of the patent system.

For the above reasons, as explained more fully below, *inter partes* review should be instituted and claims 1-10 should be found unpatentable.

A. Overview of *US982*

US982, titled "Anti-TNF Antibodies, Compositions, and Methods for the Treatment of Active Ankylosing Spondylitis," issued on May 25, 2021. The earliest possible effective filing date is February 7, 2017. EX1002, 1.

US982 explains that SC administration of TNFα[1] inhibiting drugs, such as etanercept, adalimumab, golimumab, and certolizumab pegol, for treating AS, have

[1] The scientific literature uses the terms "TNF" and "TNFα" to refer to the same tumor necrosis factor protein. *US982* uses the terms "TNF antibody," TNFα antibody," "anti-TNF antibody," and "anti-TNFα antibody" interchangeably, and this petition does as well. EX1002, 42:17-29, 14:45; EX1005 ¶51.

been "shown to be efficacious in randomized, placebo-controlled trials." EX1002, 85:60-63. *US982* further states that IV administration of golimumab for treating AS is being evaluated because "currently available IV anti-TNF α agents have limitations with respect to immunogenicity and infusion reactions, and have longer infusion times (60 to 120 minutes) compared with the proposed 30±10 minute infusions with IV golimumab" (*id.*, 86:56-63) and because "[p]atients may also prefer the maintenance dosage schedule of q8w [every 8 week] IV golimumab rather than more frequent administrations compared with SC agents" (*id.*, 86:63-65).

US982 notes that although the precise role of TNFα in AS is not fully understood, "there is already a large and mounting body of evidence that TNFα inhibition is of major therapeutic benefit in this disease." *Id.*, 85:64-67. *US982* further states that "[g]iven the known safety and efficacy of SC golimumab, it was anticipated that IV golimumab would prove efficacious with an acceptable safety profile consistent with other anti-TNF α agents in rheumatologic diseases such as RA, PsA, and AS." *Id.*, 86:29-33. *US982* notes that IV golimumab 2 mg/kg infusions administered over 30±10 minutes at Weeks 0, 4, and every 8 weeks thereafter provided substantial benefits in improving RA. *Id.*, 86:35-50.

US982 describes anti-TNF antibodies and their use in treating disorders mediated by TNFα. *E.g.*, EX1002, 2:56-64. *US982* explains that elevated

expression of TNFα has been linked to chronic inflammatory diseases such as AS, RA, and PsA, and is an important mediator of the articular inflammation and structural damage characteristic of these diseases. *Id.*, 84:42-48.

US982 broadly describes anti-TNFα antibodies as antibodies that can bind "one TNF, or specified portions, variants, or domains thereof," and can also optionally affect "at least one of TNF activity or function, such as but not limited to, RNA, DNA or protein synthesis, TNF release, TNF receptor signaling, membrane TNF cleavage, TNF activity, TNF production and/or synthesis." EX1002, 13:24-30. Anti-TNFα antibodies may thus be used "to diagnose, monitor, modulate, treat, alleviate, help prevent the incidence of, or reduce the symptoms of, at least one TNF condition, selected from, but not limited to, at least one of an immune disorder or disease, a cardiovascular disorder or disease, an infectious, malignant, and/or neurologic disorder or disease." *Id.*, 15:6-11. Immune diseases include, *inter alia*, AS, RA, and PsA. *Id.*, 38:49-54.

US982 teaches that many known modes of administration can be used to administer "pharmaceutically effective amounts of at least one anti-TNF antibody according to the present invention." *Id.*, 47:34-37. The disclosed routes of administration include "parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial," and more than 30 others. *Id.*, 48:2-11. As an example, *US982* teaches that for parenteral administration, the antibody can be

formulated, among other things, as a solution, suspension, powder, or an emulsion, and may be provided with a pharmaceutically acceptable carrier, such as water or saline. *Id.*, 47:19-29.

Regarding IV administration, the specification acknowledges that golimumab had already been successfully used to treat RA using the same dosing regimen:

> Intravenous golimumab has been definitively studied in a Phase 3 study (CNTO148ART3001) that formed the basis of approval for the treatment of RA. The CNTO148ART3001 study was a randomized, double-blind, placebo-controlled, multicenter, 2-arm study of the efficacy and safety of IV administration of golimumab 2 mg/kg infusions administered over a period of 30±10 minutes at Weeks 0, 4, and every 8 weeks (q8w) thereafter in subjects with active RA despite concurrent methotrexate (MTX) therapy. Subjects with active RA despite MTX were randomized to receive either placebo infusions or IV golimumab administered 2 mg/kg at Weeks 0, 4, and every 8 weeks through Week 24. Starting at Week 24, all subjects were treated with IV golimumab through Week 100. It was demonstrated that IV golimumab provided substantial benefits in improving RA

signs and symptoms, physical function, and health related quality of life, as well as inhibiting the progression of structural damage.

EX1002, 86:33-50.

Example 9 of the specification describes a planned multicenter, randomized, double-blind, placebo-controlled trial of golimumab to treat AS. *Id.*, 78:62-79:2. Golimumab is described as having a heavy chain of SEQ ID NO:36, a light chain of SEQ ID NO:37, and as binding to human TNFα with high affinity and specificity and neutralizing TNFα activity. *Id.*, 79:3-11. "Patients were randomized (1:1) to IV golimumab 2 mg/kg at weeks (wks) 0, 4, and every 8 wks or placebo at wks 0, 4, and 12, with crossover to golimumab at wk16." *Id.*, 105:12-18.

US982 presents preliminary efficacy and safety results through week 28. *Id.*, 106:12–107:30. Applicants concluded that "IV golimumab 2 mg/kg was efficacious in reducing signs and symptoms of AS compared with placebo. Golimumab was well-tolerated through wk28 and the safety profile was consistent with other anti-TNFs, including SC golimumab." *Id.*, col. 106-107; EX1005 ¶¶140-158.

US982 has three independent claims: 1, 4, and 7. Claims 1 and 2 are representative, and are reproduced below:

1. A method for treating a TNF related condition, wherein the TNF related condition is active ankylosing spondylitis, the method comprising:

administering a composition comprising

a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37, and

at least one pharmaceutically acceptable carrier or diluent,

wherein said composition is administered via IV infusion, and

wherein a patient treated with the composition achieves an Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment.

2. The method according to claim 1, wherein said composition is administered such that said anti-TNF antibody is administered at a dose of 2 mg/kg, administered over 30±10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.

EX1002; EX1005 ¶159. Every claim encompasses the use of an anti-TNFα antibody to achieve certain clinical results, with dependent claims that limit the dose and schedule to a dose of 2mg/kg, infused over 30±10 minutes, at Weeks 0 and 4, then every 8 weeks thereafter. In addition, every claim encompasses the use

of an anti-TNFα antibody with a "the heavy chain (HC) comprising SEQ ID NO:36 and a light chain (LC) comprising SEQ ID NO:37" (hereafter referred to as "the Claimed Sequences)." Golimumab has these sequences. EX1002, col. 109-132; EX1005 ¶¶524.

B. Prosecution History

US982 issued from U.S. Patent Application No. 16/517,592 ("the '592 Application"), filed on July 20, 2019. The '592 Application is a continuation of U.S. Patent Application No. 15/818,015, filed on November 20, 2017, now abandoned, which claims priority to U.S. Provisional Application No. 62/455,651, filed on February 7, 2017. EX1002, 1.

In an Office Action dated July 22, 2020, the examiner raised objections to the specification and claims and rejected the then-pending claims based on 35 U.S.C. §112 and §103. With respect to §103, the then-pending claims were rejected as obvious in view of *Inman* (EX1016) and *Doyle* (EX1035). EX1008, 12-15.

The examiner remarked that the claims were "broadly drawn to a method for treating a TNF related condition, wherein the TNF related condition is active Ankylosing Spondylitis" and that *Inman* teaches "treating ankylosing spondylitis using golimumab antibody and a pharmaceutically acceptable carrier by a subcutaneous injection." EX1008, 13. Although *Inman* does not teach

administering golimumab intravenously, the examiner explained that *Doyle* teaches "the administration of golimumab by subcutaneous as well as intravenous route." *Id*., 14. As such, the examiner found that it would have been *prima facie* obvious to a person of ordinary skill in the art ("POSA") at the time to administer golimumab as taught by *Doyle* for treating AS as taught by *Inman. Id.* The examiner further asserted that a POSA would have been motivated to administer golimumab by IV infusion because *Doyle* teaches that IV golimumab reduces TNFα markers to a greater extent than when administered SC. The examiner stated that a POSA would have had a reasonable expectation of success in administering golimumab IV because *Doyle* teaches administering golimumab IV and, therefore, the claimed subject matter would have been obvious over the combined teachings of *Inman* and *Doyle*. *Id*.

In response, Applicant amended the specification and claims to address the pending objections and the §112 rejection. EX1008, 17-19 (claim amendments of October 21, 2020). With respect to the §103 rejection, Applicant argued that *Inman* and *Doyle*, whether considered alone or in combination, failed to teach or suggest the recited subject matter. EX1008, 22-23 (response dated October 21, 2020).

With respect to claim 1, Applicant argued that using "a different route of administration, as taught by Inman, would not necessarily result in an ASDAS

inactive disease (<1.3) at 4 weeks or 2 weeks of treatment achieved by IV infusion as presently claimed." EX1008, 23. With respect to claim 4, Applicant argued that *Inman* "reports the clinical efficacy of subcutaneous golimumab at 14 and 24 weeks … where the change from baseline … is less than the claimed change from baseline at week 16 post-IV golimumab" and that "Doyle does not make up for the deficiencies of Inman, because Doyle does not teach or suggest that at week 16 patients treated with the anti-TNF antibody would achieve a mean change from baseline in any of the recited criteria." *Id*., 23-24. Similarly, with respect to claim 7, Applicant argued that *Inman* "reports that 60% of subjects achieve ASAS20 at 14 weeks post-subcutaneous golimumab" and that "Doyle does not make up for the deficiencies of Inman, because Doyle does not teach or suggest that ≥ 65% of patients receiving the treatment achieve ASAS20 at week 16 of treatment." *Id.*, 24.

Applicant further asserted that *Inman* and *Doyle* do not provide a reasonable expectation of success in arriving at the claimed subject matter. Applicant alleged that the *Inman* and *Doyle* do not provide a POSA "with any predictability that golimumab can be delivered by IV infusion to treat ankylosing spondylitis." EX1008, 26. Applicant further alleged that *Doyle* does not describe either (i) the effects of IV administration of golimumab on a subject with AS or (ii) any "clinical improvement from IV golimumab on any subject, let alone a subject with ankylosing spondylitis" *Id*. Applicant further contends that "Doyle describes that

inflammatory biomarkers began to increase in subjects where golimumab was administered intravenously," but that "Doyle describes the limitations of its study – small sample size that is not optimal for assessing pharmacodynamic effects." *Id*.

Finally, Applicant asserted that the claimed subject matter yielded surprising and unexpected results. For instance, Applicant argued that "[a]chieving an ASDAS inactive disease score (i.e. <1.3) after only 2 weeks or 4 weeks of IV golimumab treatment is a very surprising and unpredictable result that would not be obvious to a person skilled in the art," and that other claimed clinical results were also surprising and unexpected. EX1008, 29. As such, the "improved clinical efficacy of IV golimumab demonstrated by the present application would not be expected by a skilled artisan reading Inman and Doyle." *Id*., 30.

The examiner allowed the claims, concluding that the pending claims were non-obvious in view of the Applicant's arguments with respect to surprising results: "the combination of references would not have predicted a surprising results [sic] in treating ankylosing spondylitis in a subject in need thereof to achieve an ASDAS inactive disease (<1.3) at 4 weeks or at 2 weeks." EX1008, 38.

C. Scope and Content of the Prior Art

1. Background

RA is a chronic and progressive systemic inflammatory disease characterized by chronic inflammation of the joints that results in cartilage

damage, progressive bone erosion, and functional decline." EX1026, 160. AS and PsA are also systemic inflammatory diseases. AS is characterized by the chronic inflammation of entheses and the joints of the spine, which results in the formation of bony outgrowths on the spine and progressive functional decline. PsA is characterized by chronic inflammation of the skin, entheses (sites where tendons and ligaments connect to the bones) and joints. *Id.*

TNFα is a member of a family of structurally related cytokines, playing a pivotal role in various inflammatory processes within the body. EX1027, 27. Elevated levels of TNFα play a key role in the pathophysiology of chronic inflammatory diseases such as RA, PsA, and AS. EX1015, 18. TNFα is naturally present in the body in both soluble and membrane-bound forms. The binding of soluble or membrane-bound TNFα to the TNFα receptor is one step in the cascade of molecular interactions that cause the inflammation characteristic of RA, AS, and PsA. TNFα inhibitors decrease inflammation by acting as competitive antagonists to block the binding of soluble and membrane-bound TNFα to the TNFα receptor. EX1027, 34. The efficacy of a wide variety of TNFα inhibitors in treating and preventing RA, AS, and PsA established the importance of TNFα in the pathology of these diseases. *Id.*, 27; EX1005 ¶¶43-48.

(a) TNFα Inhibitors as Therapeutic Agents

TNFα is the single most successful antibody target molecule. Approved therapies that block the activity of TNFα were worth more than $15 billion in combined worldwide sales in 2010 alone. EX1028, 540. Before the introduction of TNFα inhibitors, few options existed for the treatment of inflammatory rheumatic diseases such as RA, and patients with RA had a significantly decreased life expectancy. EX1029, 1. Like RA, patients with AS have impaired physical function and health-related quality of life. EX1043, 1667. The development of TNFα inhibitors changed the therapeutic landscape, as they were shown to significantly decrease not only the inflammation characteristic of RA, PsA, and AS, but also the damage that the inflammation causes. EX1029, 1; EX1026, 160. TNFα inhibitors "suppress and control the inflammation driving these diseases, and thereby prevent irreversible tissue damage and disability." EX1029, 1. The TNFα inhibitors available before the earliest possible filing date of *US982*, including golimumab, were administered by both IV and SC routes. EX1026, 161. Those TNFα inhibitors, including golimumab, demonstrated clear efficacy compared to placebo, and also provided marked improvements in pain, functional ability, and inflammatory markers such as C-reactive protein. EX1030, 38.

PI2015-Simponi disclosed that TNFα has the same mechanism of action in RA, AS, and PsA (EX1015, 18), and that when golimumab is administered

subcutaneously, the same dose is effective at treating AS, RA, and PsA: 50 mg administered once per month (*id.*, 1, 4). EX1005 ¶¶49-58.

(b) Golimumab Was Approved Long Ago for the Treatment of AS

Golimumab is a human IgG1κ monoclonal antibody that binds the soluble and transmembrane bioactive forms of human TNFα, preventing it from binding to its receptors. EX1015, 18; EX1013, 285; EX1005 ¶59.

Golimumab was used to treat AS, RA, and PsA well before the earliest possible effective filing date of *US982*. EX1013, 285. SIMPONI, Janssen's SC presentation of golimumab, received FDA approval for the treatment of RA, AS, and PsA in 2009, and SIMPONI ARIA, Janssen's IV presentation of golimumab received FDA approval for the treatment of RA in 2013. EX1018, 1; EX1019, 1, 7. The efficacy and safety profile of golimumab in RA, AS, and PsA "appears to be similar to other anti-TNF agents." EX1026, 159. But golimumab was recognized as having "the potential advantage of once monthly subcutaneous administration and the possibility of both subcutaneous and intravenous administration." *Id.*, 159, 161; EX1005 ¶¶60-64.

For example, *Wong* taught a method for treating AS using TNFα inhibitors, including golimumab. EX1024, ¶¶6, 81. *Wong* taught that in a preferred embodiment, the TNFα inhibitor is administered intravenously. *Id.* ¶199. Similarly, *WO2013* taught a method for treating PsA using TNFα inhibitors,

including golimumab, and taught IV administration of the TNFα inhibitor. EX1025, 2:29-38, 31:34-35, 58:10-13; EX1005 ¶¶65; 97-99; 197-210.

As explained above, *PI2015-Simponi*, the prior art prescribing information for SIMPONI, discloses that a 50 mg dose administered by SC infusion once per month was approved to treat RA, AS, and PsA. For patients with RA, methotrexate (MTX) is administered with the golimumab, whereas for patients with PsA and AS, MTX is optional. EX1015, 4; EX1005 ¶¶60; 220-25.

Rossini reviews and updates studies looking at the efficacy, safety, and pharmacokinetics of treatment of various conditions, including AS, with golimumab. EX1013, 285. According to *Rossini*, golimumab demonstrates dose-dependent pharmacokinetics with both IV and SC administration, with steady-state concentration reached at twelve weeks. *Id.* Clearance of golimumab is dependent on body weight. *Id.*, 286.

Rossini summarizes the main Phase III studies on the use of golimumab: GO-REVEAL (PsA, 405 patients); GO-RAISE (AS, 356 patients); and GO-AFTER, GO-MORE, GO-BEFORE, and GO-FORWARD (RA, 461, 3280, 637, and 444 patients, respectively). EX1013, 287, Table 1. *Rossini* demonstrates the large number of patients, including AS patients, to whom golimumab had been successfully administered well before the earliest possible effective filing date of *US982*.

With respect to AS patients, *Rossini* notes that treatment guidance recommends the use of TNFα inhibitors "in patients with persistently high disease activity despite conventional treatments, without obligatory use of a DMARD [disease-modifying anti-rheumatic drug] before or simultaneously to the anti-TNF agent in patients with axial disease," and that "there is no evidence to support the superior efficacy of any one TNF inhibitor in axial disease and in articular/enthesial disease manifestations." *Id.*, 290.

The GO-RAISE trial "evaluated the efficacy and safety of golimumab in 356 adult patients naïve to biologic therapy, with a diagnosis of active AS … despite current or previous therapy with DMARDs or NSAIDs [non-steroidal anti-inflammatory drugs] for at least 3 months." EX1013, 290. The trial included three groups: 50 mg/month (n=138) SC golimumab; 100 mg/month (n=140) SC golimumab; and placebo (n=78). *Id.* The primary endpoint was the percentage of patients with ASAS20 (assessment in ankylosing spondylitis) response at week 14. *Id.* Secondary endpoints included: "ASAS20 response at week 24, ASAS40 response, the BASDAI [Bath Ankylosing Spondylitis Disease Activity Index] for disease activity, VAS [visual analog scale] score of back pain and night pain, the patient's global assessment, the BASFI (Bath Ankylosing Spondylitis Functional Index) for physical function, the BASMI (Bath Ankylosing Spondylitis Metrology Index) for range of motion, the SF-36 Health Survey [short form 36 item health

survey] for quality of life, and the JSEQ (Jenkins Sleep Evaluation Questionnaire) for sleep disturbance." *Id.* .; EX1005 ¶¶101-16.

Rossini reports that 59.4% of patients receiving 50 mg golimumab achieved an ASAS20 response at week 14, compared to only 21.8% of patients receiving placebo (P<0.001), and that 43.5%, 54.3%, and 15.4% of patients treated with golimumab 50 mg, 100 mg, and placebo, respectively, achieved an ASAS40 response at week 24. EX1013, 290. *Rossini* also reports that "[a]s for the BASMI scores, a significantly greater number of patients treated with golimumab 50 mg and 100 mg showed an improvement from baseline ≥1 unit at week 14" and that "[t]he overall scores for the physical and mental components of the SF-36 improved significantly (P<0.05) from baseline to weeks 14 and 24 in all golimumab treated patients." *Id.*; EX1005 ¶¶66-69, 75-79.

(c) Golimumab Had Long Been Administered Intravenously

The Center for Drug Evaluation and Research ("CDER") Administrative and Correspondence Documents for Janssen's SIMPONI ARIA BLA ("*CDER Review*") was published in September 2013. EX1034; EX1005 ¶242. The Clinical Pharmacology Review included Table 1, which shows the list of five "studies with IV dose that have been submitted during the original golimumab application (BLA125289) for its SC dosing regimen and the current golimumab application (BLA125433) for its IV dosing regimen." EX1034, 179; EX1005 ¶¶80, 243-44.

Analyzing the results of the Phase III GO-FURTHER trial referenced in *Rossini*, *Weinblatt* evaluated the efficacy of IV golimumab at a dose of 2 mg/kg in patients with active RA who were also receiving MTX. EX1012, 381. The Phase III GO-FURTHER trial included 592 patients with active disease, who were randomized 2:1 to receive IV golimumab or placebo at weeks 0 and 4, and then every 8 weeks. *Id.* *Weinblatt* taught that study agents were infused over 30±10 minutes. *Id.*, 382; EX1005 ¶¶81-82.

Weinblatt provided the following rationale for the IV dosing regimen used in the GO-FURTHER study:

> Data derived from the golimumab clinical development program indicated that maintaining drug levels close to or above the trough serum golimumab concentrations resulting from subcutaneous golimumab 50 mg every 4 weeks are important for robust and sustained ACR responses. Also using data from the golimumab program, results of simulations indicated that intravenous golimumab 2 mg/kg+MTX every 8 weeks would be anticipated to yield trough steady-state concentrations (0.28 µg/mL) comparable to subcutaneous golimumab 50 mg every 4 weeks (0.30 µg/mL). Thus,

> golimumab 2 mg/kg+MTX every 8 weeks was chosen as the dosing regimen for the current GO-FURTHER trial.

EX1012, Supplemental Online Text, 1.

Weinblatt reported that data were collected at visits scheduled for weeks 0, 2, 4, 8, 12, 14, 16, 20, and 24. EX1012, 382. *Weinblatt* further reported that "[r]esponse to golimumab was rapid" and that by week 2, there were "statistically significant treatment group differences in ACR20, ACR50, HAQ and DAS28-CRP." *Id.*, 388; *see also id.*, Figure 2. *Weinblatt* also taught the following week 2 results for golimumab+MTX compared to placebo+MTX: (a) a significant difference in ACR20 response (33.2% vs 11.7%); and (b) a significant difference in DAS28-CRP response rates (65.1% vs 19.3%). *Id.*, 383; *see also id.*, Figure 2, panel A. *Weinblatt* also states that by week 2, 65% of patients achieved a EULAR (European League Against Rheumatism) response, which is a measure of disease activity. *Id.*, 388.

The authors concluded that "[t]he addition of intravenous golimumab rapidly and significantly improved signs and symptoms in patients with active RA despite ongoing MTX, in some patients by week 2." EX1012, Abstract.

Based on these clinical trials, in 2013 FDA granted Janssen marketing approval for an IV formulation of golimumab, which Janssen marketed under the trade name SIMPONI ARIA, for the treatment of RA. *PI2013-Aria*, a version of

the approved label (prescribing information) for SIMPONI ARIA published in 2013, more than one year before the earliest possible effective filing date of the challenged claims, discloses that the dosing regimen is "2 mg/kg intravenous infusion over 30 minutes at weeks 0 and 4, then every 8 weeks." EX1032, 1, 3. *PI2013-Aria* further discloses that the golimumab solution must be diluted with 0.9% w/v sodium chloride prior to administration, and that the infusion time is 30 minutes. *Id.*, 1; EX1005 ¶100.

The pharmacokinetics of IV versus SC golimumab were also known. For example, *PI2015-Simponi* taught that "the absolute bioavailability of subcutaneous SIMPONI was estimated to be approximately 53%," while a POSA would have understood that IV-administered golimumab has a bioavailability of 100%. EX1015, 19; EX1005 ¶¶92-93. Moreover, *Zhuang* taught that 2 mg/kg IV golimumab administered once every 12 weeks results in a maximum serum concentration (C_{max}) of about 45 μg/ml compared to only about 6 μg/ml for 100 mg of golimumab administered SC at weeks 0 and 12. EX1038, 84, Table II. *Zhuang* also taught that IV golimumab, administered at weeks 0 and 12, resulted in an area under the curve ($AUC_{0\text{-}84d}$) of over 300μg·day/ml, compared to an $AUC_{0\text{-}28d}$ of only about 90 μg·day/ml for SC golimumab administered once every four weeks. *Id.* ; EX1005 ¶¶94-96.

2. Key Prior Art

(a) NCT02186873-V24 (*NCT873-V24*; EX1014)

NCT873-V24 is version 24 of a clinical trial protocol sponsored by Janssen Research titled "A Study of Golimumab in Participants with Active Ankylosing Spondylitis." It was publicly available on ClinicalTrials.gov on October 27, 2015. EX1014, 1, 4; EX1005 ¶169. Since it published more than one year before the earliest possible effective filing date of *US982*, it is prior art under post-AIA 35 U.S.C. §102(a). *Celltrion, Inc. v. Chugai*, IPR2022-00578, Paper 78 at 27-28 (Aug. 29, 2023) (a clinical trial protocol published on ClinicalTrials.gov was a prior art printed publication). Neither *NCT873-V24* nor any other version of NCT02186873 appear on the face of *US982*, and the examiner did not rely on any version of NCT02186873.

The purpose of the study reported by *NCT873-V24* was "to evaluate the efficacy of intravenously (administration of a fluid into the vein) administered golimumab 2 milligram per kilogram (mg/kg) in participants with active ankylosing spondylitis (a chronic inflammatory disease of unknown etiology that involves the sacroiliac joints, and often the axial skeleton, entheses, and peripheral joints)." EX1014, 5; EX1005 ¶170.

Under the *NCT873-V24* protocol, the AS patients were dosed according to the following schedule:

> Eligible Participants will be randomly assigned to either Treatment group 1: Placebo or Treatment group 2: Golimumab. Participants randomized to Placebo group, will receive intravenous infusions of placebo at Weeks 0, 4 and 12. At Week 16, all participants receiving placebo will begin receiving intravenous infusions of golimumab (2 mg/kg) at Weeks 16, 20 and thereafter every 8 weeks up to Week 52. Participants randomized to Golimumab group, will receive intravenous infusions of golimumab 2 mg/kg at Weeks 0, 4 and thereafter every 8 weeks up to Week 52. At Week 16, participants randomized to golimumab group will receive a placebo infusion to maintain the blind. The efficacy will be assessed primarily by measuring percentage of participants who achieve a 20 percent improvement from baseline in the assessment in ankylosing spondylitis (ASAS) at Week 16. Participant's safety will be monitored throughout the study.

EX1014, 6. In addition, Janssen tested the exact same IV dose and dosing schedule in a clinical trial to treat PsA, NCT02181673-V23 ("*NCT673-V23*") EX1011; EX1005 ¶162.

The primary outcome measure was the percentage of patients achieving a 20% improvement in Assessment in Ankylosing Spondylitis (ASAS 20) at week

14. EX1014, 7. Secondary outcome measures included: (1) Percentage of participants achieving a 40% improvement in ASAS 40 at Week 16; (2) Percentage of participants with at least 50% improvement from baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at Week 16; and (3) change from baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) score at Week 16. *Id.*, 7-8.

Thus, *NCT873-V24* teaches what the examiner found was missing from the prior art—IV administration of 2 mg/kg of golimumab for the treatment of active AS. EX1005 ¶¶170-78.

(b) PI2013-Aria (EX1032)

PI2013-Aria is the approved label for SIMPONI ARIA that was publicly available in 2013. EX1032, 1; EX1005 ¶211. Since it published more than one year before the earliest possible effective filing date of *US982*, it is prior art under post-AIA §102(a). *PI2013-Aria* does not appear on the face of *US982* and the examiner did not rely on *PI2013-Aria*.

PI2013-Aria disclosed that the FDA had approved the following golimumab dose and dosing schedule as being effective for the treatment of RA: "2 mg/kg intravenous infusion over 30 minutes at weeks 0 and 4, then every 8 weeks." EX1032, 1, 3. *PI2013-Aria* further disclosed that golimumab formulation sold by

Janssen must be diluted with 0.9% w/v sodium chloride prior to administration. *Id.*, 1.

As in *PI2015-Simponi* (EX1015), *PI2013-Aria* also describes the mechanism of action of golimumab as preventing "the binding of TNFα to its receptors, thereby inhibiting the biological activity of TNFα (a cytokine protein)." EX1032, 15. *PI2013-Aria* also presents the clinical results, such as ACR20 scores, obtained in Janssen's clinical trial of SIMPONI ARIA for the treatment of RA. *Id.*, 17. *PI2013-Simponi* further reports that "data directly comparing 2 mg/kg intravenous administration and 50 mg subcutaneous administration are not available." *Id.*, 15; EX1005 ¶¶212-219.

(c) PI2015-Simponi (EX1015)

PI2015-Simponi is the approved label for SIMPONI that was publicly available in 2015. EX1015, 1; EX1005 ¶220. Since it published more than one year before the earliest possible effective filing date of *US982*, it is prior art under post-AIA §102(a). *PI2015-Simponi* does not appear on the face of *US982* and the examiner did not rely on *PI2015-Simponi*.

PI2015-Simponi disclosed that TNFα has the same mechanism of action in RA, AS, and PsA:

> Golimumab is a human monoclonal antibody that binds to both the soluble and transmembrane bioactive forms of human

> TNFα. This interaction prevents the binding of TNFα to its receptors, thereby inhibiting the biological activity of TNFα (a cytokine protein).
>
> * **
>
> Elevated TNFα levels in the blood, synovium, and joints have been implicated in the pathophysiology of several chronic inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. TNFα is an important mediator of the articular inflammation that is characteristic of these diseases.

EX1015, 18.

PI2015-Simponi also discloses that when administered subcutaneously, the same dose of golimumab is effective at treating AS, RA, and PsA: 50 mg administered once per month. *Id.*, 1, 4; EX1005 ¶¶221-225.

(d) *Inman* (EX1016)

Inman published in 2008, more than one year before the earliest possible effective filing date of *US982*, and thus is prior art under post-AIA §102(a). EX1016, 3402; EX1005 ¶226. *Inman* described the results of a randomized, double-blind, placebo-controlled, phase III trial of golimumab, 50 mg or 100 mg, administered SC every four weeks to subjects with AS. EX1016, 3402.

Inman observed that "[g]reater proportions of patients in the golimumab groups achieved an ASAS20 response at the first assessment, 4 weeks after the first injection (Figure 3A)." *Id.*, 3406. *Inman* reported that for the 50 mg, 100 mg, and placebo groups, at week 14, 59.4%, 60%, and 21.8% of patients, respectively, achieved ASAS20 ($P < 0.001$). *Id.*, Abstract.

Figure 3A of *Inman* provides results showing that at four weeks, patients receiving SC golimumab, 50 or 100 mg, every four weeks saw improvements compared to placebo in ASAS20 (about 48%, 45%, and 12%, respectively). *Id.*, 3406, Figure 3A. Improvements in mean BASDAI score (about 4.2, 4.5, and 6.2, respectively), and means BASFI score (about 4.0, 4.0, and 5.2, respectively) were also seen at 4 weeks. *Id.*, Figures 3B-C. EX1005 ¶¶227-32.

a) *Van der Heijde* (EX1033)

Van der Heijde published in 2014 more than one year before the earliest possible effective filing date of the challenged claims and thus is prior art under post-AIA §102(a). EX1033, 1095; EX1005 ¶233. *Van der Heijde* described two-year results from a Phase III clinical trial of SC golimumab, 50 mg and 100 mg every four weeks, for the treatment of AS. EX1033, Abstract. *Van der Heijde* taught that ASDAS was used to assess the effects of golimumab therapy. *Id.* *Van der Heijde* reported that "significantly greater proportions of patients [receiving golimumab] had ASDAS inactive disease at weeks 14 and 24." *Id.*, 1097. At

week 14, 20.3% and 23.7% of patients receiving 50 and 100 mg golimumab, respectively, achieved ASDAS inactive disease compared to 2.6% of patients on placebo ($p < 0.001$), and at week 24, 27.3% and 27.2% of patients receiving 50 and 100 mg golimumab, respectively, achieved ASDAS inactive disease compared to 2.8% of patients on placebo ($p < 0.001$). *Id.*, 1099, Figure 1. The ASDAS inactive disease results in *Van der Heijde* are very similar to the ASDAS inactive disease results reported in *US982* for weeks 12, 16, 20, and 28: 19.0%, 27.6%, 28.6% and 29.5%, respectively. EX1004, col. 107, Table 9; EX1005 ¶¶ 234-41.

Van der Heijde was considered during prosecution, but neither in combination with the closest prior art, *NCT873-V24,* nor with the benefit of Dr. Fleischmann's testimony. *See generally* EX1005. Thus, the additional evidence and facts presented herein warrant reconsidering *Van der Heijde* in assessing patentability. *E.g.*, *Fresenius*, IPR2021-01025, Paper 23, 12-15.

3. Level of Ordinary Skill in the Art

A POSA would have been a medical doctor and/or clinical researcher with a Ph.D. and significant experience treating and/or researching inflammatory diseases such as RA, PsA, and AS. The POSA would have collaborated with others, including scientists skilled in related fields typically employed in pharmaceutical development, such as pharmacokineticists and formulators. EX1005 ¶¶39-42.

II. GROUNDS FOR STANDING (37 C.F.R. §42.104(A))

Petitioner certifies that *US982* is available for IPR under 37 C.F.R. §42.104(a) and that Petitioner is not barred or estopped from bringing this petition or challenging any claim of *US982* on the grounds identified herein. Petitioner has not filed a civil action challenging the validity of *US982*.

III. MANDATORY NOTICES UNDER 37 C.F.R. §42.8

Pursuant to 37 C.F.R. §§42.8(a)(1) and 42.8(b), the following mandatory notices are provided as part of this Petition.

A. Real-Party-in-Interest (37 C.F.R. §42.8(b)(1))

Accord BioPharma, Inc., Intas Pharmaceuticals Ltd., and Bio-Thera Solutions, Ltd., are the real parties in interest.

B. Related Matters (37 C.F.R. §42.8(b)(2))

Petitioner is also filing on the same day as this petition:

- IPR2026-00257, challenging US Patent No. 11,041,020 (method of treating PsA);
- IPR2026-00258, challenging US Patent No, 12,122,824 (method of treating PsA); and
- IPR2026-00259, challenging US Patent No. 12,291,566 (method of treating AS).

US982, as well as the patents being challenged in the IPRs listed above, were asserted in *Janssen Biotech, Inc., et. al. v. Accord BioPharma, Inc., et al.*, No. 1:26-cv-00222 (D. Del. Mar. 3, 2026), but Janssen and Petitioner filed a stipulation dismissing them from the litigation without prejudice. *See Janssen Biotech, Inc., et. al. v. Accord BioPharma, Inc., et al.*, No. 1:26-cv-00222 (D. Del. Mar. 17, 18, 2026), D.I. 12, 13.

C. Lead and Back-Up Counsel and Service Information (37 C.F.R. §42.8(b)(3), (4))

Lead counsel is Lora M. Green (Reg. No. 43,541). Back-up counsel are:

- Robert Cerwinski (to be admitted *pro hac vice*)
- Keith A. Zullow (Reg. No. 37,975)
- Michael Cottler (Reg. No. 79,455)
- Michael W. Johnson (Reg. No. 63,731)
- Heather M. Schneider (Reg. No. 56,484)
- Yahn-Lin (Franklin) Chu (Reg. No. 75,946)
- Counsel associated with USPTO Customer Number 192101.

Petitioner hereby consents to electronic service. Please direct all correspondence to lead and back-up counsel at the contact information below. A power of attorney accompanies this petition.

Email: lgreen@geminilaw.com

rcerwinski@geminilaw.com

kzullow@geminilaw.com

mcottler@geminilaw.com

mjohnson@geminilaw.com

hschneider@geminilaw.com

fchu@geminilaw.com

Post: GEMINI LAW LLP

32 West 39th Street, 15th Floor

New York, NY, 10018

Tel.: 301-461-9580

D. Payment of Fees Under 37 C.F.R. §42.15(a) and §42.103

The required fees are submitted herewith. If any additional fees are due at any time during this proceeding, the Office is authorized to charge such fees to Deposit Account No. 604962.

IV. OVERVIEW OF CHALLENGE AND PRECISE RELIEF REQUESTED

A. Challenged Claims and Relief Requested

Petitioner requests institution of IPR against claims 1-10 of *US982* and cancellation of these claims as unpatentable.

B. Statutory Grounds of Challenge

Each of the following prior art references and/or combinations of references renders the challenged claims unpatentable:

Ground	Claims	35 U.S.C.	References
1	1-10	§102	*NCT873-V24* (EX1014)
2	1-10	§103	*NCT873-V24* and *PI2013-Aria* (EX1032)
3	1-10	§103	*NCT873-V24, PI2013-Aria, PI2015-Simponi* (EX1015), and *Van der Heijde* (EX1033), and *Inman* (EX1016)

Petitioner's full statement of the reasons for the relief requested is set forth in greater detail below, as supported by the declaration of Dr. Roy M. Fleischmann, M.D. EX1005. Dr. Fleischmann has decades of experience as a practicing physician in the field of rheumatology, is a Master of the American College of Rheumatology, was named a "World Expert" by Expertscape based on the impact of his publications, and has also been a principal investigator in multiple Phase I-IV clinical trials of the five approved TNFα inhibitors (etanercept, infliximab, adalimumab, golimumab and certolizumab pegol). EX1005 ¶¶6-15; EX1006.

V. CLAIM CONSTRUCTION

Claim terms should be given the ordinary and customary meaning they would have to a POSA, when read in light of the specification. 37 C.F.R. §42.100(b); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*). Accordingly, the terms of the challenged claims should be given their plain and ordinary meaning. To avoid confusion, the plain and ordinary meaning of four claim terms are discussed below, none of which are defined in the patent.

A. "Treating" Should Not Be Construed as Limiting the Claimed Method

The common preamble of the independent claims describes them as being drawn to a method for treating a TNF related condition, wherein the TNF related condition is active AS. As discussed above, each of the independent claims has a dependent claim that is narrowly drawn to a dosing regimen for the IV administration of at least one isolated mammalian anti-TNF antibody, wherein that dosing regimen includes the claimed dose, infusion time, and dosing frequency. Section I.A.

Here, the term "treating" in the preamble should not be construed as limiting the claimed method because it does not modify or otherwise limit how the active step of the method is to be performed. *Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001) ("The expression does not result in a manipulative difference in the steps of the claim."); *In Re: Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018). The active step is "administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having [the Claimed Sequences]" (claims 1 and 4) or, similarly, "administering a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising [the Claimed Sequences]" (claim 7). *See, e.g.*, EX1002, claim 1. The dependent claims then specify the "safe and effective amount" to be "a dose of 2 mg/kg,

administered over 30±10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter." *Id.*, claims 2, 5, 9. "Treating" does not add any step to, otherwise result in any manipulative differences to the active step of "administering" a "safe and effective amount" of golimumab. EX1005 ¶¶512-15.

Even if "treating" were found to be a limitation, the claims and specification make clear that the term should be construed as referring to the act of administering the claimed dosing regimen to the patient, and not as requiring that the patient actually experience a clinical benefit from the treatment. This plain meaning is consistent with the claims, which make clear that not all patients who receive the claimed dosing regimen will experience those clinical benefits. For example, claim 7 recites that only ≥65% of patients achieve an ASAS20 at week 16 of treatment. That is, claim 7 acknowledges that not all patients achieve an ASAS20 at week 16. Thus, "treating" as used in the claims refers to the act of administering golimumab regardless of clinical benefit, since it encompasses administering golimumab to patients with active AS that do not experience such a benefit. EX1005 ¶¶515-16.

Further, if the preamble required that a patient actually experience a clinical benefit before falling within the scope of the claims, a POSA would be unable to determine, prior to completing the claimed treatment, whether their activity fell within the claims or not. As Dr. Fleischmann explains, when treating a particular

patient with active AS, it cannot be predicted *a priori* whether that particular patient will respond to the treatment. *Id.* ¶516.

B. The Claimed Results Do Not Limit the Claimed Methods of Treatment

Independent claims 1, 4, and 7 recite the following clinical results:

- **Claim 1:** "wherein a patient treated with the composition achieves an Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment."
- **Claim 4: "**wherein at week 16 of treatment patients treated with the anti-TNF antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Bath Ankylosing Spondylitis Functional Index (BASFI)= -2.4±2.1 Standard Deviation (SD), Bath Ankylosing Spondylitis Metrology Index (BASMI)= -0.4±0.6 SD, 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS)=8.5±7.5 SD, 36-item Short-Form Health Survey Mental Component Summary (SF-36 MCS)=6.5±9.1 SD, and Ankylosing Spondylitis Qualify of Life questionnaire (ASQoL)= -5.4±5.0 SD."
- **Claim 7:** "wherein ≥65% of patients receiving the treatment achieve Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment."

In addition, dependent claim 8, which depends from independent claim 7, adds the following clinical result:

- **Claim 8:** "wherein said ≥65% of patients that achieve ASAS20 at week 16 of treatment have a treatment difference (improvement compared to placebo) of ≥45%."

EX1002, claims 1, 4, 7, and 8.

These claimed results are merely the clinical responses reported in Tables 8 and 9 of Example 9 of *US982*, which report the results of the clinical trial disclosed in *NCT873-V24*. EX1005 ¶¶517-18. Thus, the claimed efficacy is merely the result of administering the claimed dosing regimen. It does not further limit that regimen in any way. Nor does it "result in a manipulative difference in the steps of the claim." *Bristol-Myers*, 246 F.3d at 1376.

Moreover, as explained in Section I.A, although the claims encompass administering the anti-TNFα antibody to a single patient, the results recited in the claims refer to the aggregate clinical trial results in the specification. The trial included 103 patients receiving placebo, and 105 receiving 2 mg/kg golimumab. EX1002, 106-108, Tables 8-9; EX1005 ¶¶519-20. As *US982* and its claims make clear, not all of those patients achieved the claimed results. A POSA reading claim 7 cannot glean from these aggregate results whether a particular patient will be among the 65% of patients who achieve ASAS20 at week 16 of treatment or the

35% of patients who do not. EX1005 ¶¶510-23. Similarly, less than 30% of patients achieved the ASDAS inactive disease of claim 1. EX1002, Table 9. When read in light of the clinical data in the specification, it is clear that the claims require only that a patient be administered the claimed dosing regimen—which has been shown to have the claimed clinical efficacy—not that the particular patient being treated experience the claimed clinical efficacy.

C. The Term "at least one isolated mammalian anti-TNF antibody having [the Claimed Sequences]" Encompasses Golimumab

US982 defines SEQ ID NOs 36 and 37 as the "Golimumab Heavy Chain (HC)" and "Golimumab Light Chain (LC)", respectively. EX1002, 127-131. SEQ ID NO 36 has the claimed heavy chain sequence and SEQ ID NO 37 has the claimed light chain sequence. *See id.*; EX1005 ¶524. Accordingly, the term "at least one isolated mammalian anti-TNF antibody having [the Claimed Sequences]" encompasses golimumab. EX1005, ¶524.

D. Administering "with or without" Other Drugs

Dependent claims 3, 6, and 10 add that the composition or antibody is administered "with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ)." This fails to limit independent claims 1, 4, and 7, as the word "or" causes the MTX, SSZ, or HCQ to be optional. EX1005 ¶525.

VI. GROUNDS FOR UNPATENTABILITY

Independent claims 1, 4, and 7, and dependent claim 8, are drawn to a method for treating active AS by administering a "composition comprising a safe and effective amount" of an anti-TNFα antibody having the heavy and light chains of golimumab. Dependent claims 2, 5, and 9 require a specific "safe and effective amount" of the anti-TNFα antibody: "a dose of 2 mg/kg, over 30±10 minutes, at weeks 0 and 4, and then every 8 weeks (q8w) thereafter." Dependent claims 3, 6, and 10 specify that the antibody be administered "with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ)."

As explained below, *NCT873-V24* anticipates and renders obvious these broad independent claims, as well as dependent claim 8, which do not require a specific dosing regimen. It also anticipates the specific dosing regimen required by dependent claims 2, 5 and 9. It also anticipates dependent claims 3, 6, and 10, because "with or without" MTX, SSZ or HCQ fails to further limit the claims. EX1005, Section IX.C. If it does not anticipate, *NCT873-V24* in light of other prior art would have rendered the claims obvious to a POSA. EX1005, Sections IX.D-E.

A. Ground 1: Claims 1-10 are Anticipated by *NCT873-V24*

NCT873-V24 anticipates claims 1-10 because it discloses all of the steps required by the recited method, arranged as in the claim. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008); EX1005 ¶178.

1. Claims 1, 4, and 7

(a) (Claims 1, 4, 7) "*A method for treating a TNF related condition, wherein the TNF related condition is active ankylosing spondylitis, the method comprising:*"

NCT873-V24 disclosed a clinical study to evaluate the IV administration of of a 2 mg/kg dose of golimumab in patients with active AS. *NCT873-V24* describes a clinical trial titled: "A Study of Golimumab in Participants with Active Ankylosing Spondylitis." EX1014, 1. Thus, *NCT873-V24* disclosed the preamble. EX1005 ¶¶527-30.

(b) (Claims 1 and 4) "*administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having [the Claimed Sequences], and at least one pharmaceutically acceptable carrier or diluent*," or

(Claim 7) "*administering a safe and effective amount of at least one isolated mammalian anti-TNF antibody having [the Claimed Sequences],*"

NCT873-V24 studied the efficacy of IV administration of 2 mg/kg of golimumab in patients with active AS. EX1014, 5. As explained in Section V.C. above, golimumab has the Claimed Sequences. EX1005 ¶524. In addition, challenged claims 2, 5, and 9 each further limit the safe and effective amount to IV

golimumab, 2 mg/kg, at weeks 0 and 4, and then every 8 weeks thereafter. EX1005 ¶¶544-47. *NCT873-V24* disclosed precisely this, noting that the AS patients would receive "intravenous infusions of golimumab 2mg/kg at Weeks 0, 4, and thereafter every 8 weeks." EX1014, 5-6. Thus, *NCT873-V24* meets the limitation of a safe and effective amount and meets the sequence limitations.

NCT873-V24 does not expressly state that the golimumab was dispersed in a pharmaceutically acceptable carrier or diluent as required by independent claims 1 and 4. But its disclosure must be viewed from the perspective of a POSA. *See Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991) (to anticipate, "[t]here must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention"). *NCT873-V24* disclosed that IV administration is the administration of a fluid to a vein. EX1014, 5. A POSA would have understood that a fluid containing golimumab, a protein that when isolated is a solid, necessarily contains a liquid carrier or diluent. EX1005 ¶534. Because this is a double-blind study, a POSA also would have known that the drug and placebo both have to be diluted to the same amount and infused at the same rate. *Id.* A POSA also would have been aware of *PI2013-Aria*, drawn to a Janssen IV golimumab product for treating RA, in which the golimumab is diluted with 0.9% w/v sodium chloride prior to infusion, which is a pharmaceutically-acceptable carrier or

diluent. EX1032, 1; EX1005 ¶535. Thus, a POSA would have understood that the golimumab used in *NCT873-V24* was dissolved or otherwise dispersed within a carrier or diluent suitable for human IV infusions. EX1005 ¶¶531-36.

Thus, *NCT873-V24* discloses these limitations of the independent claims. *Id*.

(c) (Claims 1 and 4) "*wherein said composition is administered via IV infusion,*"

(Claim 7) " w*herein said anti-TNF antibody is administered via intravenous (IV) infusion*,"

As discussed above, *NCT873-V24* evaluated the efficacy of 2 mg/kg of golimumab administered IV to patients with active AS. Thus, *NCT873-V24* discloses all of the limitations of the independent claims. EX1005 ¶537.

(d) (Claim 1) "*and wherein a patient treated with the composition achieves an Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment.*"

**(Claim 4) "*and wherein at week 16 of treatment patients treated with the anti-TNF antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Bath Ankylosing Spondylitis Functional Index (BASFI)=−2.4±2.1 Standard Deviation (SD), Bath Ankylosing Spondylitis Metrology Index (BASMI)=−0.4±0.6 SD, 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS)=8.5±7.5 SD, 36-item Short-Form Health Survey Mental Component Summary (SF-*

***36 MCS)=6.5±9.1 SD, and Ankylosing Spondylitis Qualify of Life questionnaire (ASQoL)=−5.4±5.0 SD.*"**

(Claim 7) "*and wherein ≥65% of patients receiving the treatment achieve Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment.*"

As discussed above in Section V.B., the clinical results recited in claims 1, 4, and 7 do not separately limit the claimed method, but merely describe the result of administering the dosing regimen of dependent claims 2, 5 and 9: 2 mg/kg of golimumab at weeks 0 and 4, and then every 8 weeks thereafter. This dosing regimen is expressly taught by *NCT873-V24*. Nothing more is required for anticipation.

Even if the efficacy further limited the claims, to the extent the dosing regimen of claims 2, 5 and 9 produces the claimed efficacy, so must the same regimen reported in *NCT873-V24*. The methods are the same, and in fact, are drawn to the same clinical trial performed on the same subjects. EX1005 ¶¶538-39. To the extent one produces the recited outcomes, so must the other. *In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990) ("It is a general rule that merely discovering and claiming a new benefit of an *old* process cannot render the process again patentable."); *In re Papesch*, 315 F.2d 381, 391 (CCPA 1963) ("a compound and all of its properties are inseparable; they are one and the same thing"); *King Pharms., Inc. v. Eon Labs., Inc.*, 616 F.3d 1267, 1276 (Fed. Cir. 2010) (Fed. Cir. 2010) (to anticipate, the prior art need only meet the claimed limitation to the

extent the patented method does); *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 809–10 (Fed. Cir. 2002) (explaining that an inventor may not obtain a patent on a process having the same steps as a prior art process, in which the new process merely identifies a new, advantageous property of the prior art process); *see also Celltrion*, IPR2022-00578, Paper 78 at 28.[2]

For this reason, *NCT873-V24* anticipates the clinical results described in independent claims 1, 4, and 7. EX1005 ¶¶538-39, 543.

[2] *But see Allergan Sales, LLC. v. Sandoz, Inc.*, 935 F. 3d 1370, 1378-79 (Fed. Cir. 2019) (Chief Judge Prost, concurring) (adding the "narrow but crucial point" that because of the term "comprising…" there is "no basis for us to conclude with any certainty that the safety and efficacy requirements of the 'wherein' clauses would always result from two doses of (1) any formulation of the combination at (2) any interval in a 24-hour period."). *Allergan* is inapposite because, as noted by Chief Judge Prost, other components of the formulation could affect the safety of the composition. In contrast, *US982* discloses a wide variety of compositions and excipients may be used (EX1002, 33:58-36:28), it does not identify any specific formulations (*id.*, Example 9), and a POSA would have understood that the safety and efficacy depend on the dose and dosing schedule of the golimumab, not the excipients (EX1005 ¶129).

2. Claim 8

Claim 8 is dependent on claim 7 and further recites: "wherein said ≥65% of patients that achieve ASAS20 at week 16 of treatment have a treatment difference (improvement compared to placebo) of ≥45%."

NCT873-V24 anticipates this claim for the same reasons as claim 7, as discussed above in Section V.A.1.. EX1005 ¶¶540-42.

3. Claims 2, 5, and 9

Claims 2, 5, and 9 depend from claims 1, 4, and 8, respectively, and further recite that the composition or antibody is administered such that "said anti-TNF-α antibody is administered at a dose of 2 mg/kg, over 30±10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter." As discussed above, *NCT873-V24* evaluated the efficacy of 2 mg/kg of golimumab administered intravenously to patients with active AS at weeks 0, 4, and every 8 weeks thereafter. Section I.C.2.a. Thus, *NCT873-V24* discloses this limitation.

Although *NCT873-V24* does not expressly state that the golimumab was infused over a period of 30±10 minutes, its disclosure must again be viewed from the perspective of a POSA. *See Scripps*, 927 F.2d at 1576. A POSA would have recognized that in *NCT873-V24* Janssen was administering SIMPONI ARIA to AS patients. The POSA would have been aware of *PI2013-Aria*, Janssen's FDA-approved label for SIMPONI ARIA, which directed that SIMPONI ARIA be

infused over a period of approximately 30 minutes. EX1032, 1. A POSA would have understood that the same dose of SIMPONI ARIA in *NCT873-V24* would be administered using the same infusion time as in the FDA-approved label. Thus, *NCT873-V24* discloses this limitation. EX1005 ¶¶544-47.

4. Claims 3, 6, and 10

Dependent claims 3, 6, and 10 further recite administering the antibody or composition "with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ)." *NCT873-V24* does not require MTX, SSX, or HCQ, and thus teaches administration "without" MTX, SSX, or HCQ. Regardless, a POSA would also know that *PI2015-Simponi* teaches that golimumab may be administered with or without MTX, SSX, or HCQ. *E.g.,* EX1015, 1, 4. Thus, *NCT873-V24* disclosed this limitation. EX1005 ¶¶548-49.

B. Ground 2: Claims 1-10 are Obvious Over *NCT873-V24* and *PI2013-Aria*

Ground 1 explains how *NCT873-V24* anticipates claims 1-10 and is incorporated by reference. Section VI.A. To the extent that a POSA would not have understood when reading *NCT873-V24* that the golimumab is dispersed in a pharmaceutically acceptable carrier or diluent as required by independent claims 1 and 4, that dispersion would have been obvious. A POSA would have understood that solid golimumab could not be infused intravenously without first being dissolved or dispersed within a liquid carrier or diluent. EX1005 ¶¶550-53, 559.

Further, *PI2013-Aria*, which is drawn to treating patients with the same IV dose of golimumab, teaches that prior to administration, the golimumab solution must be diluted with a 0.9% w/v sodium chloride solution, a pharmaceutically acceptable IV diluent. EX1032, 1. A POSA would have been motivated to use the diluent of *PI2013-Aria* when administering the IV golimumab dose in *NCT873-V24*, and would reasonably have expected success, because (1) IV dosing requires a liquid carrier or diluent, (2) *PI2013-Aria* describes the same IV dose of golimumab used for the same purpose—to treat a TNF-α related disease in humans, (3) *PI2013-Aria* is the FDA-approved prescribing information that informs doctors of the safe way to administer SIMPONI ARIA; (4) *NCT873-V24* and *PI2013-Aria* are both Janssen publications, and (5) 0.9% w/v sodium chloride solution, known as "normal saline," was the most commonly-used human IV diluent at the time. EX1005 ¶550-64. "Obviousness does not require absolute predictability of success.... *all that is required is a reasonable expectation of success.*" *In re O'Farrell*, 853 F.2d 894, 903-904 (Fed. Cir. 1988) (emphasis added). Claims 7 and 8 do not recite this limitation and are obvious based on *NCT873-V24* alone or in combination with *PI2013-Aria.* EX1005 ¶¶570; *see also id*., ¶¶554-69.

Claims 2, 5, and 9 add the limitation to the independent claims that the composition (claims 2 and 5) or antibody (claim 9) is administered such that said TNFα antibody "is administered at a dose of 2 mg/kg, over 30±10 minutes, at

weeks 0 and 4, then every 8 weeks (q8w) thereafter." To the extent that a POSA would not have gleaned from *NCT873-V24* that the golimumab is to be infused over 30±10 minutes, that infusion time would have been obvious. As explained above, *PI2013-Aria* expressly teaches this infusion time for the same golimumab dose and schedule. Section I.C.2.b. A POSA would have been motivated to use the infusion time of *PI2013-Aria* with the dosing regimen of *NCT873-V24* for the same reasons explained above with respect to the diluent, and would have reasonably expected success with it, since FDA had approved this infusion time for the dosing schedule common to both references. EX1005 ¶¶571-75.

Claims 3, 6, and 10 add the limitation that the anti-TNF-α antibody is "administered with or without" MTX, SSX, or HCQ. Because, as explained in Section V.D., the optional choice of administering MTX, SSX, or HCQ does not limit the claims, and *NCT873-V24* discloses administration without MTX, SSX, or HCQ, these claims are also obvious. EX1005 ¶¶576-80.

As explained in Section V.B., the clinical results recited in claims 1, 4, 7 and 8 do not comprise additional limitations of the claimed method, but merely describe the results produced by the claimed method. Although neither *NCT873-V24* nor *PI2013-Aria* disclose the claimed clinical outcomes, a POSA following the teachings of *NCT873-V24* would have observed precisely the claimed results because the trial cited in Example 9 of *US928* is the same clinical trial of *NCT873-*

V24. EX1005 ¶¶566-69. Janssen cannot render the otherwise-obvious method of claims 1-10 non-obvious by merely reciting the results of that method, even if it produces somewhat better results than expected. *In re Kubin*, 561 F.3d 1351, 1357-58 (Fed. Cir. 2009) (concluding that, as the prior art rendered the protein obvious, it also rendered obvious its binding properties, as it would remove from the public "that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art) (citing *In re Wiseman*, 596 F.2d 1019, 1023 (CCPA 1979)); *id.* at 1357 (citing *Gen. Elec. Co. v. Jewel Incandescent Lamp Co.,* 326 U.S. 242, 249 (1945) ("It is not invention to perceive that the product which others had discovered had qualities they failed to detect.")); *Woodruff*, 919 F.2d at 1578; *Papesch*, 315 F.2d at 391; *Catalina Mktg.*, 289 F.3d at 809–10.

For the above reasons, *NCT873-V24* and *PI2013-Aria* would have rendered claims 1-10 obvious to a POSA. EX1005 ¶¶554-80; *see also* Section VI.A..

C. Ground 3: Claims 1-10 Are Obvious Over the Combination of *NCT873-V24*, *PI2013-Aria*, *PI2015-Simponi, Van der Heijde*, and *Inman*

Grounds 1 and 2 are hereby incorporated by reference. As discussed above in Section VI.A., *NCT873-V24* teaches the only active step required by the claims: administering 2 mg/kg of golimumab intravenously to a patient with active AS at weeks 0 and 4, and then every 8 weeks thereafter. *PI2013-Aria* taught the use of a carrier or diluent, as well as the 30-minute infusion time, and *PI2015-Simponi*

taught that golimumab was effective for treating RA, AS, and PsA at the same SC dose and regimen. Sections I.C.2.b-c. This is where the obviousness analysis should end. But to the extent that the clinical outcomes recited in claims 1, 4, 7, and 8 are deemed to be material additional limitations, the combination of *NCT873-V24*, *PI2013-Aria*, *PI2015-Simponi*, *Van der Heijde*, and *Inman* would have rendered those results obvious. EX1005 ¶¶581-82. The efficacy parameters set forth in the claims recite nothing more than the standard clinical endpoints that had been assessed in connection with golimumab and other TNF-α therapies. Further, the particular claimed values of those endpoints are not clinically distinguishable from the efficacy reported in the prior art for golimumab and other TNF-α therapies.

1. Claims 1-3

Claim 1 states the following clinical result: "achiev[ing] an Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment." A POSA would have reasonably expected this clinical result from the combination of *NCT873-V24*, *PI2013-Aria*, *PI2015-Simponi*, *Van der Heijde*, and *Inman*.

Van der Heijde taught that during a Phase III study of subcutaneous golimumab for the treatment of AS, ASDAS was used to assess the effects of golimumab therapy. EX1033, Abstract. *Van der Heijde* reported that

"significantly greater proportions [receiving golimumab] had ASDAS inactive disease at weeks 14 and 24." *Id.*, 1097. At week 14, 20.3% and 23.7% of patients receiving 50 and 100 mg golimumab, respectively, achieved ASDAS inactive disease compared to 2.6% of patients on placebo ($p < 0.001$), and at week 24, 27.3% and 27.2% of patients receiving 50 and 100 mg golimumab, respectively, achieved ASDAS inactive disease compared to 2.8% of patients on placebo ($p < 0.001$). *Id.*, Figure 1. From these results, a POSA would have expected at least some patients to have achieved ASDAS inactive disease by week 4. EX1005 ¶¶583-87.

In addition, *Inman*, which reports the results of a phase III clinical trial of golimumab, 50 mg or 100 mg, administered SC every four weeks to subjects with AS, observed rapid improvement in ASAS20. EX1005 ¶¶588-89. At four weeks, when the first assessment was made: "[g]reater proportions of patients in the golimumab groups achieved an ASAS20 response at the first assessment, 4 weeks after the first injection (Figure 3A)." EX1016, 3406. Figure 3A shows that at four weeks, patients receiving SC golimumab, 50 or 100 mg every four weeks, saw improvements compared to placebo in ASAS20 (about 48%, 45%, and 12%, respectively). *Id.*, Figure 3A. Improvements in mean BASDAI score (about 4.2, 4.5, and 6.2, respectively), and mean BASFI score (about 4.0, 4.0, and 5.2, respectively) were also seen at 4 weeks. *Id.*, Figure 3B, 3C. The efficacy observed

at 4 weeks would have confirmed the POSA's expectation that at least some patients would have achieved ASDAS inactive disease by week 4. EX1005 ¶¶590-92.

A POSA also would have been aware of *Weinblatt's* teaching that IV golimumab for treating RA, administered using the same dosing regimen as taught in *NCT873-V24*, rapidly and significantly improved signs and symptoms in RA patients, in as little as two weeks in some patients. EX1012, Abstract. *Weinblatt* taught that by week 2, there were "statistically significant treatment group differences in ACR20, ACR50, HAQ and DAS28-CRP," reporting that 33.2% of golimumab subjects achieved ACR20 compared to 11.7% of placebo patients, and DAS28-CRP results were 65.1% compared to 19.3%, and that by week 2, 65% of patients achieved a EULAR (European League Against Rheumatism) response, which is a measure of disease activity. *Id.*, 382, 383, Figure 2, panel A, 388. This, too, would have confirmed the POSA's expectation of efficacy at week 4 for at least some patients. EX1005 ¶593.

Claim 1 only requires that "a patient treated with the composition achieves" an ASDAS inactive disease at week 2 or 4 of treatment. Thus, rather than requiring that a minimum percentage of patients must achieve ASDAS inactive disease at week 2 or 4, claim 1 only requires that at least one patient out of the treated patients achieves that result. Consistent with the claim language is the fact

that *US982* reports that under 10% and under 15% of subjects achieve ASDAS inactive disease at week 2 and week 4, respectively. EX1002, Table 9; EX1005 ¶¶591-95. Moreover, claim 1 does not limit the baseline ASDAS of the patient that achieves ASDAS inactive disease, and a POSA would have known that a subject with a baseline ASDAS closer to 1.3, who is encompassed by the claim, would be more likely to more quickly achieve ASDAS inactive disease than a subject with a higher baseline ASDAS. EX1005 ¶¶591-95.

Based on (1) the percentage of patients (>20%) that *Van der Heijde* reports as achieving ASDAS inactive disease at 14 weeks, (2) the rapid results seen in *Inman* when treating AS with SC golimumab, (3) the rapid results seen when using IV golimumab for the treatment of RA, with the same dose and regimen as taught in *NCT873-V24*, (4) the FDA approval of golimumab to treat AS at the same doses as treating RA and PsA, and (5) a POSA's knowledge that IV golimumab has a higher bioavailability, C_{max}, and AUC than SC golimumab, a POSA would reasonably have expected at least some patients receiving IV golimumab as taught in *NCT873-V24* would achieve ASDAS inactive disease by week 2 or week 4. EX1005 ¶¶592-593.

A POSA would have been motivated to combine the teachings of *NCT873-V24*, *PI2015-Simponi*, *Van der Heijde*, and *Inman* because they all relate to using golimumab for the treatment of AS. A POSA would have been motivated to

combine these teachings with *PI2013-Aria* because *NCT873-V24* and *PI2013-Aria* are both Janssen publications that teach administering golimumab with the same route of administration (IV), at the same dose (2 mg/kg) and frequency (week 0 and 4, and then every 8 weeks thereafter), for the treatment of a TNF related condition (AS and RA, respectively). EX1005 ¶594. *E.g.*, EX1011, 4 (Janssen tested the exact same IV dose and dosing schedule in a clinical trial to treat PsA).

A POSA would have had a reasonable expectation of success for the same reasons as set forth in Section VI.B., above, *i.e.*, because the prior art teaches that (1) golimumab achieves results quickly, (2) the claimed IV golimumab dosing regimen had been approved by FDA as safe and effective for treating RA, (3) TNFα has the same mechanism of action in RA, AS, and PsA and all three are effectively treated by inhibiting TNFα, and (4) SC golimumab, in doses lower than those of the claimed IV regimen, had been approved as safe and effective for treating active AS. EX1005 ¶¶594-95.

Claim 2 depends from claim 1, and claim 3 depends from any of claims 1-2. Claims 2 and 3 do not recite any additional clinical results and therefore would have been obvious to a POSA for the same reasons as claim 1. EX1005 ¶¶583, 617.

Accordingly, the combination of *NCT873-V24*, *PI2013-Aria*, *PI2015-Simponi*, *Van der Heijde*, and *Inman*, renders claims 1-3 obvious. *In re O'Farrell*, 853 F.2d at 903-904.

2. Claims 4-6

Claim 4 recites that the anti-TNF-α antibody achieves a specified mean change from baseline in one or more criteria selected from the group consisting of: BASFI (Bath Ankylosing Spondylitis Functional Index), BASMI (Bath Ankylosing Spondylitis Metrology Index), SF-36 PCS (36-item Short-Form Health Survey Physical Component Summary), SF-36 MCS (Mental Component Summary), and ASQoL (Ankylosing Spondylitis Quality of Life questionnaire).

NCT873-V24 expressly discloses assessing BASFI scores at Week 16 as a secondary endpoint. EX1014, 8. Thus, *NCT873-V24* discloses one of the outcomes recited in claim 4, but does not report the actual results. Moreover, *Van der Heijde*, which reported on the results of a phase III clinical trial of golimumab, 50 mg or 100 mg, administered SC every four weeks to subjects with AS, reported, *inter alia*, mean changes in SF-36 PCS compared to baseline at 14 and 24 weeks. EX1033, 1098, Table 2; EX1005 ¶¶596-600.

The claimed mean changes from baseline in claim 4 are modified by a specific standard deviation ("SD") which makes them very broad. For example, the change in SF-36 PCS from baseline recited in claim 4 is of 8.5±7.5 SD, where

SD is the standard deviation. As Dr. Fleischmann explains, these standard deviations indicate a very large spread in the results seen in individual patients. EX1005 ¶¶597-98. Thus, a mean change in SF-36 PCS of 8.5±7.5, in which the SD is almost the same as the change in SF-36 PCS, means that 68% of subjects would have a change in SF-36 PCS of 1.0 to 16.0. EX1005 ¶¶117-20, 274 (citing EX1017).

Van der Heijde reports in Table 2 that at week 14, the mean change in SF-36 PCS in patients receiving 50 or 100 mg golimumab was 8.8±9.6 SD and 8.9±9.8 SD, respectively ($p < 0.001$). EX1033, 1098 (Table 2) (*see also* 24 week mean changes from baseline of 9.6±10.6 SD and 9.2±10.3 SD, respectively ($p < 0.001$)). Given that *Van der Heijde* reports mean changes in SF-36 PCS at week 14 of 8.8 and 8.9 for 50 and 100 mg SC doses, respectively, which are higher than the claimed mean changes, and given that a POSA would have known that IV golimumab has a higher bioavailability, C_{max}, and AUC than 100 mg SC golimumab, a POSA would have reasonably expected that an IV dose of 2 mg/kg of golimumab would achieve a mean change in SF-36 PCF of at least 8.5±7.5. EX1005 ¶¶599-601.

As discussed above in Section VI.B., the combination of *NCT873-V24* and *PI2013-Aria* renders obvious the method of intravenously administering golimumab at a dose of 2 mg/kg at weeks 0 and 4, then every 8 weeks thereafter.

The results recited in claim 4 merely describe the result of that method. But to the extent that the results are deemed to impose a further limitation, the combination of *NCT873-V24*, *PI2013-Aria*, *PI2015-Simponi*, *Van der Heijde*, and *Inman* renders obvious those results. EX1005 ¶¶596-603; *see also* Section VI.C.1.

Claim 5 depends from claim 4, and claim 6 depends from any of claims 4-5. Claims 5 and 6 do not recite any additional clinical results and therefore would have been obvious to a POSA for the same reasons as claim 4. EX1005 ¶¶571-75.

Accordingly, the combination of *NCT873-V24*, *PI2013-Aria*, *PI2015-Simponi*, *Van der Heijde*, and *Inman*, renders claims 4-6 obvious. EX1005 ¶¶596-603.

3. Claims 7-10

Claim 7 recites that ≥65% of patients receiving the treatment achieve ASA20 at week 16 of treatment, and claim 8 is dependent on claim 7, and specifies that said ≥65% of patients that achieve ASAS20 at week 16 of treatment achieve a treatment difference (improvement compared to placebo) of ≥45%.

While *NCT873-V24* does not provide results of the disclosed clinical trial, the result of administering IV golimumab as taught in that trial would have been the same as the clinical responses of that trial as disclosed in Table 8 of *US982*. EX1005 ¶¶604-05. Furthermore, *NCT873-V24* teaches that the primary outcome measure of the study is the percentage of patients achieving ASAS20 at Week 16.

EX1014, 7. Thus, *NCT873-V24* would have motivated a POSA to assess the efficacy of the claimed method in exactly the same way as described in the claims. EX1005 ¶604-06.

In addition, *Inman* reported ASAS20 results, at week 14, for patients administered subcutaneous golimumab, 50 mg and 100 mg. EX1016, 3407, Table 2. *Inman* reported that for the 50 mg, 100 mg, and placebo groups, at week 14, 59.4%, 60%, and 21.8% of patients, respectively, achieved ASAS20 ($P < 0.001$). *Id.*, Abstract. *Inman* concluded that "Golimumab was effective and well tolerated in a large cohort of patients with AS." *Id.*, 3402. EX1005 ¶¶607-08.

As explained above, *Inman* teaches that golimumab was effective and that about 60% of patients receiving golimumab achieved ASAS20 at week 14 compared to only 21.8% of patients receiving placebo. While the percentage of patients achieving ASAS20 at week 14 reported in *Inman* for 50 mg SC golimumab is a lower number than the claimed percentage of patients achieving ASAS20 with IV golimumab at week 16, a POSA would have known that both *Inman* and *PI2015-Simponi* teach that the SC dose was very effective for treating AS. EX1005 ¶¶608-610. In addition, a POSA would have appreciated that 2 mg/kg of IV golimumab would produce greater average drug exposure—i.e., bioavailability, C_{max} and AUC—than SC golimumab. A POSA therefore would not have been surprised if some additional individual patients treated with IV

golimumab achieved ASAS20 at week 16 with a higher percentage showing improvement compared to placebo. EX1005 ¶¶609-611.

Moreover, a POSA would have known that head-to-head clinical studies would be necessary to determine whether IV golimumab outperforms SC golimumab. In the absence of such head-to-head data, a POSA would not have viewed as clinically meaningful the small differences between the results observed in the SC and IV studies, both of which demonstrated efficacy by satisfying their primary endpoints. EX1005 ¶¶609-615.

Janssen also did a meta-analysis comparing the efficacy and safety of IV golimumab with other biologics, as well as SC golimumab in patients with RA. EX1050; EX1005 ¶¶249-60, 724. That meta-analysis confirmed that these therapies had equivalent efficacy, concluding that there were "no statistical differences in efficacy between IV golimumab and IV infliximab, abatacept, or SC golimumab in terms of ACR 20, ACR 50, and ACR 70 at Weeks 12 to 16 and Weeks 24 to 26, HAQ-DI at 12–16 weeks, and DAS 28 at Weeks 12 to 16 and Weeks 24–26." EX1050, 6; EX1005 ¶609.

In summary, *NCT873-V24* would have motivated a POSA to apply the claimed dosing regimen to patients with active PsA, and to measure the resulting efficacy using the claimed parameters. The results of this obvious method do not confer patentability. *Kubin*, 561 F.3d at 1357; *Woodruff*, 919 F.2d at 1578;

Papesch, 315 F.2d at 391; *Catalina Mktg.*, 289 F.3d at 809–10. As explained above in Sections VI.C.1-2., a POSA would have been motivated to follow the combined teachings of *NCT873-V24* and *PI2013-Aria*, and *PI2015-Simponi* and, having done so, would have arrived at the claimed method. The claimed results do confer patentability to this otherwise-obvious method. EX1005 ¶¶615-16.

Claims 9 and 10, which depend from any of claims 7-8, do not recite any additional clinical results and therefore would have been obvious to a POSA for the same reasons as claims 7-8. EX1005 ¶617.

Accordingly, the combination of *NCT873-V24*, *PI2013-Aria*, and *PI2015-Simponi*, *Van der Heijde*, and *Inman*, renders claims 7-10 obvious. EX1005 ¶¶581-617.

D. Objective Indicia of Non-Obviousness

During prosecution, Janssen argued that the claimed invention yielded surprising and unexpected results. EX1008, 27-30 (Office Action Response dated October 21, 2020). In particular, Janssen compared the recited IV golimumab with SC golimumab and represented that "[e]ach of the clinical measures at 16 weeks post-IV golimumab was surprisingly and unexpectedly improved over the same clinical measures at 14 and 24 weeks post-subcutaneous golimumab as reported by Inman." *Id*., 29-30. Further, Janssen represented that "[a]chieving an ASDAS inactive disease score (i.e. <1.3) after only 2 weeks or 4 weeks of IV golimumab

treatment is a very surprising and unpredictable result that would not be obvious to a person skilled in the art." *Id*., 29. Based on this data, Janssen argued that the results achieved would not have been expected based on the references cited by the examiner, including *Inman* and *Doyle*. Such representations directly contributed to the indication of allowance. EX1008, 40 (Examiner Interview Summary) (Janssen represented that intravenous injection provided improved performance over subcutaneous injection and the examiner found these arguments "to be persuasive").

The unexpected results presented by Janssen during prosecution do not support patentability of the *US982* claims for at least three reasons. First, purported unexpected results must be presented relative to the closest prior art. *In re Baxter Travenol Labs*., 952 F.2d 388, 392 (Fed. Cir. 1991) ("when unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art"). Here, *Inman* and *Van der Heijde* were not the closest prior art. As demonstrated in the grounds of challenge herein, the closest prior art is the clinical protocol *NCT873-V24*. *NCT873-V24* used the same 2 mg/kg IV golimumab as claimed in *US982* and indicated that clinical outcomes claimed in *US982* would be measured during the clinical trial. Janssen, however, did not present *NCT873-V24* to the examiner. Janssen did include Example 9 in *US982*, with over 30 columns describing the clinical trial and

preliminary results for the clinical trial, the protocol for which had been published more than a year before *US982*'s earliest possible effective filing date. *NCT873-V24* provided a limitation that Janssen argued distinguished the claims over *Inman* and *Van der Heijde*, "treat[ing] ankylosing spondylitis using golimumab by IV infusion at dose 2 mg/kg" administered at weeks 0 and 4 and every 8 weeks thereafter. EX1010, 75; EX1005 ¶¶618-24.

Second, Janssen argued during prosecution that IV golimumab provided surprising results relative to SC golimumab. EX1009, 29. For example, in comparison to ASDAS results seen with SC golimumab, Applicant argued that "[a]chieving an ASDAS inactive disease score (i.e. <1.3) after only 2 weeks or 4 weeks of IV golimumab treatment is a very surprising and unpredictable result that would not be obvious to a person skilled in the art," and that other claimed clinical results were also surprising and unexpected. EX1008, 29. But as demonstrated by statements by the FDA in the *CDER Review*, it appears as if Janssen never directly compared SC administration to IV administration. EX1005 ¶625; EX1034, 114; EX1032, 15 ("Data directly comparing 2mg/kg intravenous administration and 50 mg subcutaneous administration are not available."); *In re De Blauwe,* 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual evidence."); EX1005 ¶625.

Third, Janssen presented statements to the FDA that contradict what it told the USPTO. As explained above in Section IV.C.3., Janssen never did any comparative, head-to-head studies of IV and SC golimumab. Thus, under Federal Regulations or FDA Guidance, it could not truthfully say that one is superior to the other. Indeed, during FDA review of SIMPONI ARIA for RA, FDA did not allow Janssen to simply rely on a pharmacokinetic comparison of SIMPONI ARIA with SIMPONI to establish efficacy, and complained that Janssen's failure to conduct a head-to-head comparison between SIMPONI and SIMPONI ARIA made its approval determination "more difficult by a lack of data derived from a direct comparison of the to-be-marketed IV dose regimen and the SC regimen." EX1034, 114; EX1005 ¶¶626-27. In the wake of FDA's complaint, Janssen cannot argue to the USPTO that IV golimumab is unexpectedly superior to SC golimumab to obtain allowance of the claims. *See Duties of Disclosure and Reasonable Inquiry During Examination, Reexamination, and Reissue, and for Proceedings Before the Patent Trial and Appeal Board,* USPTO (July 29, 2022) ("[I]n PTAB proceedings, parties should not take a position about the patentability of challenged claims that is inconsistent with positions taken in submissions to other Government agencies regarding the same subject matter.")

Petitioner reserves the right to respond to any allegations that objective indicia support the validity of the challenged claims.

E. Discretion Under § 325(d) and § 314

Consistent with the guidance provided by "FAQs for Interim Processes for PTAB Workload Management," Petitioner does not present affirmative arguments as to discretionary denial. Should Patent Owner elect to file a Discretionary Denial Brief, Petitioner will present arguments in its Opposition to that brief.

VII. CONCLUSION

For the reasons set forth above, claims 1-10 of *US982* are unpatentable. Petitioner requests that an *inter partes* review of these claims be instituted and that the claims be cancelled.

Respectfully submitted,

Dated: March 20, 2026

/ Lora M. Green /

Lora M. Green, Lead Counsel
Reg. No. 43,541

VIII. APPENDIX – LIST OF EXHIBITS CITED

Exhibit No.	Description
1001	U.S. Patent No. 11,041,020 to Harrison et al. (June 22, 2021) ("*US020*")
1002	U.S. Patent No. 11,014,982 to Harrison et al. (May 25, 2021) ("*US982*")
1003	U.S. Patent No. 12,122,824 to Harrison et al. (Oct. 22, 2024) ("*US824*")
1004	U.S. Patent No. 12,291,566 to Harrison et al. (May 6, 2025) ("*US566*")
1005	Declaration of Dr. Roy M. Fleischmann in Support of IPR Petition
1006	Dr. Roy M. Fleischmann *curriculum vitae*
1007	Excerpts from prosecution history of U.S. Application No. 16/517,594, now U.S. Patent No. 11,041,020
1008	Excerpts from prosecution history of U.S. Application No. 16/517,592, now U.S. Patent No. 11,014,982
1009	Excerpts from prosecution history of U.S. Application No. 17/320,490, now U.S. Patent No. 12,122,824
1010	Excerpts from prosecution history of U.S. Application No. 17/237,650, now U.S. Patent No. 12,291,566
1011	U.S. National Library of Medicine, ClinicalTrials.gov, NCT02181673, "*A Study of Golimumab in Participants with Active Psoriatic Arthritis*" (Version 23, January 8, 2016), available at https://clinicaltrials.gov/study/NCT02181673? ("*NCT673-V23*")
1012	M. E. Weinblatt, et al., *Intravenous golimumab is effective in patients with active rheumatoid arthritis despite methotrexate therapy with responses as early as week 2: results of the phase 3, randomised, multicentre, double-blind, placebo-controlled GO-FURTHER trial*, 72 ANN RHEUM DIS 381-389 (2013) ("*Weinblatt*")
1013	M. Rossini, et al., *Why golimumab in the treatment of psoriatic arthritis, ankylosing spondylitis and rheumatoid arthritis*?, 66 REUMATISMO 4:285-303 (Apr. 2014) ("*Rossini*")

Exhibit No.	Description
1014	U.S. National Library of Medicine, ClinicalTrials.gov, NCT02186873, "*A Study of Golimumab in Participants with Active Ankylosing Spondylitis*" (Version 24, October 27, 2015), available at https://clinicaltrials.gov/study/NCT02186873? ("*NCT873-V24*")
1015	*SIMPONI (golimumab) injection, for subcutaneous use*, FOOD AND DRUG ADMINISTRATION (June 2015), https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125289s024lbl.pdf ("*PI2015-Simponi*")
1016	R. D. Inman, et al., *Efficacy and Safety of Golimumab in Patients With Ankylosing Spondylitis,* 58 ARTHRITIS & RHEUMATISM 11:3402-3412 (Nov. 2008) ("*Inman*")
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Exhibit No.	Description
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Exhibit No.	Description
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IX. CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. §42.24(d), the undersigned certifies that this Petition complies with the type-volume limitation of 37 C.F.R. §42.24(a). The word count application of the word processing program used to prepare this Petition indicates that the Petition contains 13,718 words, excluding the parts of the brief exempted by 37 C.F.R. §42.24(a).

Respectfully submitted,

Dated: March 20, 2026

/Lora M. Green/
Lora M. Green, Lead Counsel
Reg. No. 43,451

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§42.6(e) and 42.105(a), this is to certify that I caused to be served a true and correct copy of the foregoing Petition for Inter Partes Review (and accompanying Exhibits 1001-1019, 1022, 1024-1030, 1032-1044, 1050-1052) by overnight courier (Federal Express Priority Overnight Delivery), on this 20th day of March, 2026, on the Patent Owner at the correspondence address of the Patent Owner Counsel as follows:

Riverside Law LLP/ J&J
175 Strafford Avenue
Suite 100
Wayne, PA

Respectfully submitted,

Dated: March 20, 2026

/Ashley Cheung/
Ashley Cheung
Paralegal for Petitioner's Counsel