

Filed on behalf of: Janssen Biotech, Inc.

Entered: June 29, 2026

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.

IPR2026-00258
Patent No. 12,122,824

PATENT OWNER'S PRELIMINARY RESPONSE

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TABLE OF ABBREVIATIONS**Medical terms**

PsA	Psoriatic arthritis
IV	Intravenous
MTX	Methotrexate
AS	Ankylosing spondylitis
RA	Rheumatoid arthritis
SC	Subcutaneous
SpA	Spondyloarthritis
TNF, TNF α	Tumor necrosis factor alpha
UC	Ulcerative colitis

Clinical endpoints and indices

HAQ-DI	Health Assessment Questionnaire Disability Index
SF-36 MCS	Short-Form Health Survey Mental Component Summary
SF-36 PCS	Short-Form Health Survey Physical Component Summary
vdH-S	Total Modified van der Heijde-Sharp Score
ACR	American College of Rheumatology

EXHIBIT LIST

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2001	Prosecution History for U.S. Patent No. 11,041,020 B2 (“’020 Patent PH”) (EXCERPT)
2002	Prosecution History for U.S. Patent No. 12,122,824 B2 (“’824 Patent PH”) (EXCERPT)
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2501	Declaration of Luke Brennan (“Brennan Decl.”) (HC-AEO MATERIAL AND REDACTED VERSIONS)
2502	Declaration of Thao Marzullo (“Marzullo Decl.”) (HC-AEO MATERIAL AND REDACTED VERSIONS)

I. Introduction

Patent Owner Janssen Biotech, Inc. (“Janssen”) respectfully requests that the Director deny institution of the Petition for inter partes review filed by Accord Biopharma, Inc., Intas Pharmaceuticals Ltd., and Bio-Thera Solutions, Ltd. (collectively, “Petitioners”) challenging U.S. Patent No. 12,122,824 B2 (the “’824 Patent”). The ’824 Patent protects methods for treating active psoriatic arthritis (“PsA”) by intravenous (“IV”) administration of golimumab, an antibody against tumor necrosis factor (“TNF” or “TNF α ”).

Petitioners’ challenge fails at the outset because they have failed to establish that their primary reference is prior art. All grounds rely on NCT673-V23 (Ex.1011), an online summary of a clinical trial protocol. Although the document states “Viewing V23 (2016-01-08),” it bears a “Last Update” date in December 2017. Ex.1011, 1-2. That notation does not satisfy Petitioners’ burden to establish NCT673-V23 as prior art. The record contains no evidence that the purported “V23” content was publicly accessible on January 8, 2016. Nor do Petitioners show (assuming it was on the website), that V23 was meaningfully indexed so a POSA would have found it.

But even if NCT673-V23 were prior art—and it is not—Petitioners’ challenge still fails because NCT673-V23 does not disclose the claimed clinical endpoints recited in the ’824 Patent. Further, NCT673-V23 omits key criteria defining the

relevant patient population. Petitioners resort to inherent anticipation to supply the missing limitations but fail to demonstrate that the missing limitations are necessarily present in NCT673-V23. That failure is dispositive. Petitioners cannot establish that the clinical study would necessarily have achieved the claimed clinical endpoints. Petitioners have not met—and cannot meet—their burden here.

Next, Petitioners' obviousness theories are driven by hindsight and fail to disclose all claim limitations, even if the asserted references were combined. Petitioners attempt to extrapolate efficacy from a different disease (rheumatoid arthritis, "RA") and a different route of administration (subcutaneous, "SC"). But material differences in disease biology and drug pharmacokinetics foreclose that extrapolation.

The contemporaneous literature recognized that RA and PsA "differ substantially" such that their treatments "should therefore also differ." Ex.2091 (Schett 2011), 1. Likewise, the FDA explained that SC and IV golimumab are "separate and distinct products because they have different pharmacokinetic characteristics, dosing regimens, and product presentations." Ex.1034, 127. In line with this guidance, Janssen developed distinct SIMPONI[®], SC golimumab, and SIMPONI ARIA[®], IV golimumab, products. Consistent with those concerns, prior attempts to extrapolate from SC to IV administration of golimumab in ulcerative

colitis (“UC”) failed, and efforts to develop an IV golimumab product for UC were abandoned.

Because Petitioners fail to demonstrate a reasonable likelihood of prevailing as to any claim, Janssen respectfully requests the Director deny institution.

II. Background

A. Psoriatic Arthritis

PsA is a chronic inflammatory disease that belongs to a family of diseases called spondyloarthritis (“SpA”). Ex.2054 (“Haroon”) ¶ 33. PsA affects ligaments, tendons, and several joints, including axial (i.e., spinal) and peripheral joints (i.e., fingers and toes). Ex.2069 (Fitzpatrick’s Dermatology), 427. PsA patients also experience enthesitis (inflammation in the points where connective tissues attach to bone) and skin lesions, including psoriasis. *Id.* PsA may lead to serious impairment of patients’ mobility and quality of life. Ex.2072 (Gladman 2003), 34.

Patients with PsA often have elevated TNF levels. But as Petitioners acknowledge, “the precise role of TNF α in PsA is unknown.” Ex.1005 (Fleischmann Decl.) ¶ 125.

Clinicians assess PsA treatment success using validated, disease-specific clinical endpoints. Haroon ¶¶ 26-32. They include:

- Health Assessment Questionnaire Disability Index (HAQ-DI): a functional index assessing a patient’s physical ability;

- Enthesitis: a measure of inflammation at tendons, ligaments, or joints, commonly around the lower extremities and pelvis;
- Dactylitis: a measure of swelling at fingers or toes;
- Short-Form Health Survey Mental Component Summary (SF-36 MCS): a standardized tool measuring psychological and emotional well-being;
- Short-Form Health Survey Physical Component Summary (SF-36 PCS): a standardized tool measuring how physical health limits the ability to do common activities;
- American College of Rheumatology 20 (ACR20): a composite functional index based on joint measurements and a patient's self-assessment of disease activity;
- Total modified vdH-S (vdH-S): a measurement of damage in several joints based on x-ray images.

Id. The total modified vdH-S score was developed specifically to assess the treatment of PsA patients. Ex.2097 (van der Heijde 2005), ii63.

B. A POSA Would Have Recognized That RA and PsA Are Fundamentally Different Diseases

Petitioners' invalidity arguments rest on a superficial comparison between RA and PsA. *See, e.g.*, Pet. 14 ("Like RA, patients with PsA have impaired physical function and health-related quality of life, and since PsA patients are more commonly younger and male, they have constraints on productivity similar to or

worse than patients with RA.”). But a POSA would have understood that RA and PsA are distinct diseases with materially different biology and clinical characteristics.

RA and PsA involve distinct immunological pathways. The human immune system has two main branches that operate differently. The innate immune system is the body's first line of defense; it responds quickly to a broad range of threats but does not target any one of them specifically. Haroon ¶ 34. The adaptive immune system responds more slowly, but it recognizes specific antigens, mounts a targeted attack against them, and “remembers” them for the future. *Id.*

RA is primarily driven by the adaptive immune system. *Id.* PsA, by contrast, is associated with dysregulation of the innate immune system, meaning the disease arises from the broader, faster responses to immune triggers. *Id.*; Ex.2080 (Lories & Baeten 2009), S-12 (“In contrast to RA, specific adaptive autoimmune features are not found in SpA synovitis, where the inflammation seems to be dominated by innate immune cells such as macrophages, polymorphonuclear cells, and mast cells.”). This distinction is reflected in TNF biology: in RA, TNF is produced by B cells (a fundamental component of the adaptive immune system), whereas in PsA, TNF is associated with macrophages and mast cells. Haroon ¶ 34; Ex.2080, S-12; *see also* Ex.2069, 427 (“many features of the pathogenesis of [PsA], including the importance of CD8 T cells, ... are highly distinct from features of [RA]”). Thus, treatment is different for RA and PsA.

The immunological differences are also reflected in whether patients have rheumatoid factor antibodies in their blood. Haroon ¶ 35. Patients with RA typically test positive for rheumatoid factor. *Id.* Rheumatoid factor is an important product of B cells in RA patients and informs RA treatment. *Id.* By contrast, rheumatoid factor is typically absent in the SpA family of diseases, which includes PsA and ankylosing spondylitis (“AS”). *Id.*

The genetic underpinnings of the two diseases are also distinct. By the priority date, PsA was strongly associated with the genetic marker HLA-B27 and other genes underlying psoriasis, while RA was associated with different markers: HLA-DR1 and -DR4. Ex.2068 (FitzGerald 2015), Abstract; Ex.2071 (Fugger & Svejgaard 2000), Abstract.

RA and PsA also affect different tissues. In RA, inflammation occurs primarily in synovial tissue and peripheral joints, and axial involvement is rare. Ex.2080, S-10-11. PsA patients, by contrast, experience a different variety of symptoms, including enthesitis (inflammation involving tendons and ligaments), fasciitis (inflammation in connective tissue), dactylitis (inflammation in fingers and toes), new bone formation, and skin inflammation. Ex.2069, 427.

RA and PsA patient populations also differ markedly, which Petitioners and their expert fail to address. RA predominantly affects female patients, while the impact of PsA is evenly distributed across male and female patients. Ex.2099

(van Vollenhoven 2009), 2; Ex.2073 (Gladman 2005), ii14. The populations also differ in body composition, which affects weight-based dosing. PsA patients typically have a higher body mass index (“BMI”), whereas RA patients have a broader distribution of BMIs. Haroon ¶ 37.

Petitioners and their expert largely ignore these critical distinctions between PsA and RA, offering only a superficial overview of each disease. *See* Pet. 13; Ex.1005 ¶¶ 44-46. That omission is significant. The fundamental differences between PsA and RA directly shape treatment strategies and therapeutic options available for each disease. *See* Haroon ¶¶ 41-46.

C. A POSA Would Have Understood That RA and PsA Require Different Treatment Strategies

A POSA would have understood that the differences between RA and PsA also extended to treatment. For example, a POSA would have known that RA patients must receive concomitant methotrexate (“MTX”) with Simponi, whereas the same is not true for PsA patients. Haroon ¶ 45.

A POSA at the time of the invention likewise understood that PsA has a distinct inflammatory pattern, requiring treatment to address disease activity across multiple tissue compartments. *See supra* Section II.B. As a result, RA and PsA required—and continue to require—different therapeutic approaches. For instance, a POSA would have recognized that tocilizumab (“TCZ”) was approved for RA but not PsA. *See* Ex.2061 (ACTEMRA[®] (tocilizumab) Label), 1. Studies also

concluded that rituximab (a B cell therapy commonly used in RA), was not an appropriate treatment for SpA patients. Ex.2083 (Mease 2012), 2235. And not every anti-TNF agent effective in RA was effective in PsA at the same dosage at the time of the claimed invention, and are still different today: infliximab requires a higher dose for PsA than for RA. *See* Ex.2062 (REMICADE® (infliximab) Label), 1. As for clinical measures of PsA treatment, the PsA-specific total modified vdH-S score expands the joints evaluated compared to its RA predecessor. Ex.2097, ii63.

The contemporaneous literature explained that because RA and PsA “differ substantially in their patterns of bone and cartilage damage.... Goals and strategies to prevent and treat structural damage should therefore also differ.” Ex.2091, 1; Ex.2072, 29 (“PsA and RA are distinct diseases, and the efficacy and safety of an agent in RA cannot necessarily be equated with efficacy and safety in PsA.”).

D. A POSA Would Have Understood That SC and IV Administration Are Different

Petitioners' invalidity theory also treats SC and IV administration of golimumab as equivalent. *See, e.g.*, Pet. 4 (relying on “equivalent efficacy of SC and IV golimumab for RA”). Yet a POSA at the time of the invention would have understood that SC and IV are fundamentally different delivery routes with materially distinct pharmacokinetic and pharmacodynamic (“PK/PD”) profiles.

Compared with SC administration, IV administration can produce markedly higher peak serum concentration (“C_{max}”), greater drug exposure (area under the

curve, or “AUC”), lower trough levels (“C_{min}”), and substantially greater variability in blood levels over time. Haroon ¶¶ 50-57. These pharmacokinetic differences arise in part because SC dosing uses the patient’s subcutaneous tissue as a “reservoir,” permitting more gradual absorption and release into the circulation. *Id.* ¶ 55. By contrast, IV administration delivers the full dose directly into the bloodstream at once, while the drug is simultaneously subject to systemic elimination. *Id.*

A POSA would have understood that differences in PK/PD would preclude any meaningful extrapolation of safety and efficacy from SC to IV administration. The FDA expressly recognized this difference and explained:

We consider the IV and SC formulations of golimumab to be two separate and distinct products because they have different pharmacokinetic characteristics, dosing regimens, and product presentations, despite having the same drug substance.

Ex.1034, 127. For example, there were significant concerns that IV administration could require higher dosing, increase drug exposure, and create a “possible dose-related increase in serious adverse events including malignancy.” *Id.*; *see also* Haroon ¶¶ 51-52. These safety concerns were so pronounced that the European Medicines Agency denied regulatory approval for IV golimumab for RA, despite the established use of SC golimumab for the same indication. Ex.2052 (EMA Withdrawal), 6. The EMA believed that the differences with IV administration,

including potentially six-fold higher $C_{\max}$ and three-fold greater AUC, “raise[d] uncertainty regarding the safety profile versus SC administration that remain[ed] for long term treatment.” *Id.* 59.

Despite higher overall drug exposure, IV administration also raised concerns of reduced efficacy because trough concentrations in the blood may be lower. Haroon ¶ 55; Ex.2086 (Naganuma), 332 (“subcutaneous golimumab may be more useful because efficacy with single-dose intravenous golimumab was lower than the efficacy observed for subcutaneous golimumab”).

In 2015, Rutgeerts conducted a randomized, placebo-controlled trial of SC and IV golimumab for UC. Ex.2089 (“Rutgeerts 2015”). The authors selected IV dosing regimens that were “expected to provide comparable systemic drug exposure” to SC administration. *Id.* 509-10. Even with that attempted apples-to-apples comparison, the authors concluded: “Efficacy with single-dose golimumab IV induction was lower than expected and less than observed in the SC induction study.” *Id.* 504. Increasing the IV dose did not help because “no dose-response was observed.” *Id.* 512. Although IV administration produced higher peak drug levels, the authors concluded that “peak serum golimumab concentration is not a dominant driver of efficacy.” *Id.* 511.

The results reported by Rutgeerts 2015 (Ex.2089) foreshadowed the ultimate failure of IV golimumab for UC, even though SC golimumab was already approved

and widely used for the same indication. Ex.1015, 1 (SC golimumab for UC); Haroon ¶¶ 53-57. Experience with SC administration did not translate to IV, and efforts to bridge that gap were abandoned. Ex.2070 (Flamant), 882 (“the proportion of patients achieving clinical response was low and studies with intravenous golimumab administration were not subsequently continued”); Ex.2058 (ClinicalTrials.gov ID NCT00488774), 1 (“Protocol was cancelled by company based on overall efficacy[.]”); *see also* Ex.2093 (Steiner), 410-11; Ex.2086, 332; Ex.2095 (Ungar & Kopylov 2016), 244.

III. The Asserted References

A. NCT673-V23 (Ex.1011)

NCT673-V23 is an online summary of a clinical trial protocol investigating IV golimumab in PsA patients. Ex.1011. Aside from version information and study locations, its substantive disclosure spans just three pages. *Id.* As discussed below, Petitioners failed to establish that NCT673-V23 qualifies as prior art. *See infra* Section VII.A.

NCT673-V23 contains no data regarding the claimed clinical endpoints. Ex.1011. It discloses only the existence of an ongoing clinical trial, omitting key aspects of the protocol. *Id.* 5.

Compared with the '824 Patent, NCT673-V23 fails to disclose key clinical trial parameters, including:

- Eligibility by meeting Classification Criteria for Psoriatic Arthritis (“CASPAR”) criteria (Ex.1003 ('824 Patent), 77:55-58, 86:4-7, 88:14-16);
- Eligibility criteria for at least one of the PsA subsets (*id.* 88:22-25);
- Permissive concurrent use of MTX and requisite stable dosage “at least 4 weeks prior to the first administration of” IV golimumab (*id.* 84:27-31, 89:61-90:2);
- Prohibition of concurrent topical or ultraviolet therapy (*id.* 90:18-20, 98:44-65); and
- Efficacy calculation based on an intent-to-treat analysis and early escape procedures (*id.* 80:28-34, 96:7-23).

Petitioners also concede that “NCT673-V23 does not expressly state that the golimumab was dispersed in a pharmaceutically acceptable carrier or diluent” or “that the golimumab was infused over a period of 30±10 minutes.” Pet. 43, 45.

Petitioners incorrectly assert that the “claims issued only because Janssen failed to disclose NCT673-V23 to the examiner.” *Id.* 1. In fact, NCT673-V23 is substantially the same as NCT02181673 History (Ex.2049) and cumulative of Hoffman (Ex.1036) and Doyle (Ex.1035). *See* Paper 11 at 13-16. NCT02181673 History disclosed the same study as NCT673-V23, including the same clinical trial identifier. Ex.2049 (NCT02181673 History), 1. Doyle is a 2010 published study describing the results of a Phase I trial of SC and IV golimumab on the inflammatory

biomarkers. Ex.1035. Hoffman is a 2008 U.S. Patent Application Publication describing the use of TNF inhibitor adalimumab in PsA patients. Ex.1036.

B. PI2015-Simponi (Ex.1015)

PI2015-Simponi is the prescribing information for Simponi, Janssen's SC formulation of golimumab to treat RA, PsA, AS, and UC. Ex.1015. As discussed below, Petitioners failed to establish that PI2015-Simponi qualifies as prior art. *See infra* Section VII.B.

PI2015-Simponi discloses neither the claimed IV administration route nor achieving the claimed clinical endpoints. Haroon ¶ 79. Instead, it reports inferior ACR20 endpoints both at and after the 14-week mark recited in the '824 Patent claims. *Compare* Ex.1015, 26 (Table 4), *with* Ex.1003, 141:1-6 (independent claim 5). It also reports inferior HAQ-DI endpoints after the 14-week mark recited in the claims. *Compare* Ex.1015, 28, *with* Ex.1003, 139:45-55 (independent claim 1). Nor does it disclose other claimed clinical endpoints, including dactylitis, SF-36 MCS and PCS, and vdH-S score.

Other references considered by the Examiner, including Cohen (Ex.2038), disclose substantially the same thing as PI2015-Simponi. *See* Paper 11 at 16. Both report clinical endpoints of the same Phase III trial in RA and concern SC administration of golimumab in accordance with the labels. Ex.2038, -001; *compare id.* -004, *with* Ex.1032, 17-18 (Table 2).

C. PI2013-Aria (Ex.1032)

PI2013-Aria is the prescribing information for Simponi Aria, Janssen's IV formulation of golimumab to treat RA. Ex.1032. As discussed below, Petitioners failed to establish that PI2013-Aria qualifies as prior art. *See infra* Section VII.B.

PI2013-Aria does not disclose PsA or the claimed clinical endpoints. It is directed exclusively to RA, a disease understood to have a different pathology from PsA and to require a different treatment strategy. *See supra* Sections II.B-C. A POSA would have recognized that RA and PsA "differ substantially in their patterns of bone and cartilage damage" and therefore "[g]oals and strategies to prevent and treat structural damage should therefore also differ." Ex.2091, 1.

Other references considered by the Examiner, including Cohen (Ex.2038), disclose substantially the same thing as PI2015-Simponi. *See* Paper 11 at 16. Both concern IV administration of golimumab for RA in accordance with the label. Ex.2038, 1.

D. GO-REVEAL (Exs.1041-1044)

Petitioners refer to four separate articles as GO-REVEAL. All four references describe the clinical endpoints of a clinical trial of SC golimumab to treat PsA. Exs.1041-1044. GO-REVEAL does not disclose IV administration of golimumab.

GO-REVEAL also fails to disclose numerous clinical endpoints at the timepoints recited in the claims. Kavanaugh 2009 reports inferior HAQ-DI

endpoints after the 14-week mark recited in the claims of the '824 Patent. *Compare* Ex.1041, 980, *with* Ex.1003, 139:45-55 (independent claim 1). It also reports inferior ACR20 endpoints at the week-14 mark recited in the claims. Haroon ¶ 119; *compare* Ex.1041, 979, *with* Ex.1003, 141:1-6 (independent claim 5). Kavanaugh 2012 reports inferior total modified vdH-S scores at the 24-week mark recited in the claims. Haroon ¶ 116; *compare* Ex.1042, 2509, *with* Ex.1003, 140:34-37 (independent claim 3).

The Examiner considered Kavanaugh 2009 (Ex.1041) and Kavanaugh 2014 (Ex.1044) during prosecution of the '824 Patent. Ex.2002, -108, -255 (IDS).

E. WO213 (Ex.1025)

WO213 describes methods of treating PsA via SC adalimumab administration. While it states that its teachings “are representative of a TNF α inhibitor,” all working examples are limited to adalimumab. Ex.1025, 80:14-18. It does not disclose IV administration of golimumab. Haroon ¶ 85.

WO213 reports inferior HAQ-DI endpoints both before and after the 14-week mark recited in the '824 Patent claims. *Compare* Ex.1025, 117-18 (Table 42), *with* Ex.1003, 139:45-55 (independent claim 1). It also reports inferior total modified vdH-S endpoints at the 24-week mark recited in the claims. *Compare* Ex.1025, 127-28 (Table 44), *with* Ex.1003, 140:34-37 (independent claim 3).

During prosecution of the '824 Patent, the Examiner considered references substantially similar to WO213, including *Hoffman* (Ex.1036).

IV. The Patented Invention

The '824 Patent, titled “Anti-TNF Antibodies, Compositions, and Methods for the Treatment of Active Ankylosing Spondylitis,”¹ discloses “methods utilizing anti-TNF antibodies having a heavy chain (HC) comprising SEQ ID NO:36 and a light chain (LC) comprising SEQ ID NO:37 for use in the safe and effective treatment of active Psoriatic Arthritis (PsA).” Ex.1003, Abstract. SEQ ID NOS:36 and 37 correspond to golimumab. *Id.* 76:56-57.

The '824 Patent describes a multicenter, randomized, double-blind, placebo-controlled clinical trial of IV golimumab to treat PsA. *Id.* 76:45-118:24 (Example 9). The study showed marked improvement in PsA across multiple clinical endpoints. For example, patients achieved significant clinical endpoints ($\geq 65\%$ achieving ACR20) at week 14. *Id.* 114:1-115:18 (Tables 8-9).

The priority date of the '824 Patent is January 30, 2017 (*see id.* Cover (60) (Related U.S. Application Data)), which Petitioners do not dispute. *See* Pet. 5; Ex.1005 ¶ 32.

¹ The reference to AS in the title is a clerical error. The '824 Patent concerns methods of treating PsA.

The '824 Patent has three independent claims.² Independent claim 1 of the '824 Patent recites:

1. A method for treating a tumor necrosis factor alpha (TNF- α) related condition, wherein the TNF- α related condition is active psoriatic arthritis, the method comprising: administering to a subject having active psoriatic arthritis a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF- α antibody comprising:

a. a heavy chain (HC) complementary determining region (CDR) 1 comprising an amino acid sequence of SEQ ID NO: 1;

b. a HC CDR2 comprising an amino acid sequence of SEQ ID NO: 2; wherein position 1 of SEQ ID NO: 2 is phenylalanine, position 2 of SEQ ID NO: 2 is methionine, position 3 of SEQ ID NO: 2 is serine, position 4 of SEQ ID NO: 2 is tyrosine, position 10 of SEQ ID NO: 2 is lysine, position 11 of SEQ ID NO: 2 is tyrosine, and position 17 of SEQ ID NO: 2 is glycine;

² For purposes of the Patent Owner's Preliminary Response, Janssen will focus on the independent claims to demonstrate why Petitioners have failed to meet their burden. Janssen reserves the right to present further arguments and evidence on all the '824 Patent claims.

- c. a HC CDR3 comprising an amino acid sequence of SEQ ID NO: 3; wherein position 4 of SEQ ID NO: 3 is isoleucine, position 5 of SEQ ID NO: 3 is alanine, and position 9 of SEQ ID NO: 3 is asparagine;
- d. a light chain (LC) CDR1 comprising an amino acid sequence of SEQ ID NO: 4; wherein position 7 of SEQ ID NO: 4 is tyrosine;
- e. a LC CDR2 comprising an amino acid sequence of SEQ ID NO: 5; and
- f. a LC CDR3 comprising an amino acid sequence of SEQ ID NO: 6, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via intravenous (IV) infusion, wherein said anti-TNF- α antibody is administered at a dose of 2 mg/kg, over 30 $\pm$ 10 minutes, at Weeks 0 and 4, then every 8 weeks (q8w) thereafter, and wherein at week 14 of treatment patients treated with the anti-TNF- α antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Health Assessment Questionnaire Disability Index score (HAQ-DI)=-0.60 $\pm$ 0.53 SD, enthesitis=-1.87 $\pm$ 1.75 SD, dactylitis=-7.8 $\pm$ 8.57 SD, Short-Form Health Survey Physical Summary score (SF-36 PCS)=8.65 $\pm$ 7.60 SD, and Short-Form Health Survey Mental Component Summary score (SF-36 MCS)=5.33 $\pm$ 9.95 SD.

Ex.1003, 139:13-55 (claim 1).

Independent claim 3 of the '824 Patent recites:

- 3. A method for treating a TNF- α related condition, wherein the TNF- α related condition is active psoriatic arthritis, the method comprising: administering to a subject having active psoriatic arthritis a

composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF- α antibody comprising:

- a. a heavy chain (HC) complementary determining region (CDR) 1 comprising an amino acid sequence of SEQ ID NO: 1;
- b. a HC CDR2 comprising an amino acid sequence of SEQ ID NO: 2; wherein position 1 of SEQ ID NO: 2 is phenylalanine, position 2 of SEQ ID NO: 2 is methionine, position 3 of SEQ ID NO: 2 is serine, position 4 of SEQ ID NO: 2 is tyrosine, position 10 of SEQ ID NO: 2 is lysine, position 11 of SEQ ID NO: 2 is tyrosine, and position 17 of SEQ ID NO: 2 is glycine;
- c. a HC CDR3 comprising an amino acid sequence of SEQ ID NO: 3; wherein position 4 of SEQ ID NO: 3 is isoleucine, position 5 of SEQ ID NO: 3 is alanine, and position 9 of SEQ ID NO: 3 is asparagine;
- d. a light chain (LC) CDR1 comprising an amino acid sequence of SEQ ID NO: 4; wherein position 7 of SEQ ID NO: 4 is tyrosine;
- e. a LC CDR2 comprising an amino acid sequence of SEQ ID NO: 5; and
- f. a LC CDR3 comprising an amino acid sequence of SEQ ID NO: 6, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via IV infusion, wherein said anti-TNF- α antibody is administered at a dose of 2 mg/kg, over 30 $\pm$ 10 minutes, at Weeks 0 and 4, then every 8 weeks (q8w) thereafter, and wherein at week 24 of treatment patients treated with the anti-TNF- α antibody achieve a mean change from baseline in total modified van der Heijde-Sharp score (vdH-S)=-0.36 $\pm$ 0.144 SE.

Id. 139:59-140:37 (claim 3).

Independent claim 5 of the '824 Patent recites:

5. A method for treating a TNF- α related condition, wherein the TNF- α related condition is active psoriatic arthritis, the method comprising: administering to a subject having active psoriatic arthritis a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF- α antibody comprising:

a. a heavy chain (HC) complementary determining region (CDR) 1 comprising an amino acid sequence of SEQ ID NO: 1;

b. a HC CDR2 comprising an amino acid sequence of SEQ ID NO: 2; wherein position 1 of SEQ ID NO: 2 is phenylalanine, position 2 of SEQ ID NO: 2 is methionine, position 3 of SEQ ID NO: 2 is serine, position 4 of SEQ ID NO: 2 is tyrosine, position 10 of SEQ ID NO: 2 is lysine, position 11 of SEQ ID NO: 2 is tyrosine, and position 17 of SEQ ID NO: 2 is glycine;

c. a HC CDR3 comprising an amino acid sequence of SEQ ID NO: 3; wherein position 4 of SEQ ID NO: 3 is isoleucine, position 5 of SEQ ID NO: 3 is alanine, and position 9 of SEQ ID NO: 3 is asparagine;

d. a light chain (LC) CDR1 comprising an amino acid sequence of SEQ ID NO: 4; wherein position 7 of SEQ ID NO: 4 is tyrosine;

e. a LC CDR2 comprising an amino acid sequence of SEQ ID NO: 5; and

f. a LC CDR3 comprising an amino acid sequence of SEQ ID NO: 6, wherein said anti-TNF- α antibody is administered via intravenous (IV) infusion, wherein said 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, and wherein $\geq 65\%$ of patients receiving the treatment achieve ACR20 at week 14 of treatment.

Id. 140:41-141:6 (claim 5).

The Examiner allowed the claims over the same or substantially similar prior art as advanced by Petitioners, including NCT02181673 Study History (Ex.2049), Cohen (Ex.2038), Kavanaugh 2009 (Ex.1041), Kavanaugh 2014 (Ex.1044), and Hoffman (Ex.1036). Ex.2002, -099, -103-04, -108, -255. The Examiner rejected the pending claims as anticipated by Hoffman and as obvious over Hoffman combined with Doyle (Ex.1035). *Id.* -033-38, -127-33. After fully considering the issues, however, the Examiner found the claims patentable over this prior art based on the “unexpected and surprising” results achieved by Janssen’s invention. *Id.* -153-54.

V. Person of Ordinary Skill in the Art

The definition of a POSA depends on the art of the claimed invention. *See, e.g., Daiichi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254, 1257 (Fed. Cir. 2007). Factors considered in defining a POSA include, but are not limited to: (1) the inventor’s education level; (2) the type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity in which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in

the field. *Env't Designs, Ltd. v. Union Oil Co. of Cal.*, 713 F.2d 693, 696-97 (Fed. Cir. 1983).

Petitioners propose defining a POSA as a medical doctor or Ph.D. clinical researcher with “significant experience treating and/or researching inflammatory diseases such as RA, PsA, and AS,” together with collaborators involved in pharmaceutical development. Pet. 32. Petitioners’ formulation suggests that a POSA could have significant experience in any one of RA, PsA, or AS (or an arbitrary combination), while failing to specify the level of experience required with any particular disease. Janssen agrees that a POSA may include a medical doctor or Ph.D. clinical researcher, but Petitioners are mistaken to require significant treatment and/or research experience in RA without experience in SpA. Haroon ¶ 19. Petitioners’ inclusion of “significant experience” with RA reflects hindsight and improperly conflates RA-based prior art (Ex.1032) with the claimed invention.

The development of therapies for the SpA family of diseases (including AS and PsA) differs significantly from that for RA. PsA and AS are typically rheumatoid factor seronegative, associated with dysregulation of the innate immune system, and characterized by pathologic new bone formation. By contrast, RA is rheumatoid factor seropositive, driven by adaptive immunity, and marked by erosive loss of bone and cartilage. Haroon ¶¶ 33-40; *see also supra* Section II.B. These differences lead to different treatment strategies. Ex.2091, 1 (“Goals and strategies

to prevent and treat structural damage should therefore also differ.”); *see also supra* Section II.C.

A POSA, properly defined, would include a medical doctor or Ph.D. clinical researcher with experience treating and/or researching SpA (including AS and PsA). Haroon ¶ 19. Although some clinicians treat both SpA and RA, the focus should be on expertise in SpA not RA. *Id.* A POSA would have collaborated with a team experienced “in pharmaceutical development, such as pharmacokineticists and formulators,” a qualification on which the parties agree. Pet. 32; Haroon ¶ 19. Because the invention involves applying clinical trial data, a POSA also would have worked with a team member experienced in clinical trial design and biostatistics. Haroon ¶ 19.

In any event, as explained below, Petitioners’ invalidity arguments fail under either definition of a POSA.

VI. Claim Construction

Claim terms “are generally given their ordinary and customary meaning,” as understood by a POSA, read in the context of the surrounding claim language and specification. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (citations omitted). Claim terms need only be construed if they are in controversy, and only as needed to resolve the controversy. *See Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999).

Petitioners ask the Board to disregard multiple claim terms while tacking unsupported modifiers onto others. As explained below, those arguments lack merit because each disputed claim term substantively limits claim scope.³

A. Petitioners' Construction of "Administering to a Subject" Lacks Intrinsic and Legal Support

Petitioners incorrectly assert that the limitation of independent claims 1, 3, and 5 reciting "administering to a subject having active psoriatic arthritis" should be construed to mean "administration to a single subject." Pet. 36. Petitioners provide no intrinsic or extrinsic basis to support this interpretation beyond their expert's nearly verbatim opinion. *Id.* (citing Ex.1005 ¶ 396). This construction openly contradicts well-established Federal Circuit precedent and the claim language. Instead, the claims of the '824 Patent should be construed as "administering to *one or more subjects* having active psoriatic arthritis."

³ Patent Owner reserves the right to advocate for claim construction if the Director institutes review. For example, Patent Owner does not presently address Petitioners' claim construction of "at Least One Isolated Mammalian Anti-TNF Antibody Comprising [the Claimed CDR Sequences]" because it is not material to Petitioners' patentability challenges at this stage. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

The Federal Circuit has repeatedly articulated a general rule that “an indefinite article ‘a’ or ‘an’ in patent parlance carries the meaning of ‘one or more’ in open-ended claims containing the transitional phrase ‘comprising.’” *Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342-43 (Fed. Cir. 2008) (quoting *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000)). The Court provides “extremely limited” exceptions to the rule, which require evidence of “a clear intent” to limit the article. *Id.*

Petitioners fail to identify any language in the patent or elsewhere that evinces any intent to limit the phrase to “a single subject.” In fact, the claim language itself demonstrates the absence of such intent. Each independent claim of the '824 Patent recites a limitation “wherein ... *patients* treated with the anti-TNF- α antibody” or “wherein ... *patients* receiving the treatment” achieve certain clinical endpoints. Ex.1003, 139:45-47, 140:34-35, 141:4-5 (independent claims 1, 3, and 5) (emphases added). The specification similarly describes treating multiple subjects. *See, e.g., id.*, 42:59-63 (describing the TNF inhibitor’s “ability to treat *patients*”) (emphasis added); *see also id.* 76:45-118:24 (Example 9); *see* Haroon ¶ 88. As open-ended claims that contain the transitional phrase “comprising” and explicitly concern the administration of treatment to *one or more* subjects, the independent claims of the '824 Patent fall squarely within the Court’s rule in *Baldwin* and *KCJ*.

Thus, Petitioners' construction should be rejected. Consistent with case law and the patent itself, the correct construction is "administering to *one or more subjects* having active psoriatic arthritis."

B. "Treating ... Active Psoriatic Arthritis" in the Preamble Is Limiting

A preamble is limiting when necessary to give life, meaning, and vitality to the claim. *Griffin v. Bertina*, 285 F.3d 1029, 1033 (Fed. Cir. 2002). Courts have found a preamble limiting where, without it, the essence of the invention has no purpose beyond mere academic exercise. *See, e.g., id.* (finding preamble to be a necessary limitation where the steps of the treatment become empty language without purpose or context in its absence).

Here, the preamble is limiting, consistent with the Federal Circuit's holding in *Eli Lilly & Co. v. Teva Pharmaceuticals International GmbH*, 8 F.4th 1331 (Fed. Cir. 2021). In that case, the Federal Circuit affirmed the Board's finding that the preamble "[a] method for treating headache in an individual" was limiting as a statement of intended purpose, explaining that "we have generally construed statements of intended purpose in such method claims as limiting." *Id.* at 1335, 1340-42; *see also Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003); *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003).

The structural parallel between *Eli Lilly* and the claims here is striking. Just as the preamble in *Eli Lilly* recited a method “for treating headache,” here the ’824 Patent claims recite a method “for treating a tumor necrosis factor alpha (TNF- α) related condition, wherein the TNF- α related condition is active psoriatic arthritis.” Ex.1003, 139:13-15. Both preambles identify the specific therapeutic purpose that gives meaning to the claimed administration steps; without that purpose, the claims recite administering a drug without therapeutic context. Haroon ¶ 90.

Later claim limitations, which refer back to the method for treating PsA, confirm the preamble’s significance. For example, claim 1 later refers to “patients *treated*” and “at week 14 of *treatment*.” Ex.1003, 139:45-48 (emphases added). The preamble is limiting because “treating ... active psoriatic arthritis” provides context and an antecedent basis for those later claim limitations. *In re Fought*, 941 F.3d 1175, 1178 (Fed. Cir. 2019) (“We have repeatedly held a preamble limiting when it serves as antecedent basis for a term appearing in the body of a claim.” (citing cases)).

Finally, the written description consistently emphasizes that treatment of active PsA is fundamental to the invention. *See, e.g.*, Ex.1003, Abstract (“for use in the safe and effective treatment of active Psoriatic Arthritis (PsA)”), 1:17-21 (Field of the Invention) (“methods utilizing [golimumab] for use in the safe and effective treatment of active Psoriatic Arthritis (PsA)”), 2:60-64 (Summary of the Invention) (“The present invention provides [golimumab] for use in the safe and effective

treatment of active Psoriatic Arthritis[.]”). The preamble is limiting because it embodies the essence of the claimed invention. *See Eli Lilly*, 8 F.4th at 1342 (“Thus, the preambles are the portions of the claims that embody the essence of the claimed invention—methods for treating vasomotor symptoms.”).

Petitioners’ reliance on *Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001) and *In re Copaxone Consolidated Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018), is misplaced. In both cases, the preamble term was not limiting because the body of the claim set out the complete invention and the method would have been performed “the same way regardless” of the treatment term. *Bristol-Myers*, 246 F.3d at 1375 (citation omitted); *see also Copaxone*, 906 F.3d at 1023. That is not the case here, where the body of the claim requires administering “a safe and effective amount” of golimumab to achieve specified clinical endpoints. The treatment of active PsA is necessary to give meaning to these limitations. *See Eli Lilly*, 8 F.4th at 1342-43.

C. The Claimed Clinical Endpoints Are Limiting

Petitioners attempt to evade claim scope by disregarding clinical endpoints recited in the “wherein” clauses of the claims. A patent claim defines the precise scope of a claimed invention. *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950 (Fed. Cir. 2006). Thus, “claims are interpreted with an eye toward giving effect to all terms in the claim.” *Id.* (citations omitted).

The Federal Circuit's decision in *Allergan Sales, LLC v. Sandoz, Inc.*, confirms that "wherein" clauses reciting safety and efficacy results have limiting effect. 935 F.3d 1370, 1378-79 (Fed. Cir. 2019). "When a 'whereby' or 'wherein' clause states a condition that is material to patentability, it cannot be ignored to change the substance of the invention." *Id.* at 1376 (cleaned up) (quoting *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329 (Fed. Cir. 2005) (per curiam)).

The intrinsic record establishes that the claimed clinical endpoints are material to patentability. The Examiner repeatedly relied on those endpoints to distinguish the claims from the prior art. For example, the Examiner withdrew the initial rejection over Hoffman and Doyle because Janssen's invention "shows surprising results in improving disease activity and physical function, skin psoriasis clearance, reduction in dactylitis and enthesitis, HRQoL and inhibition of structural progression." Ex.2002, -153-54. Similarly, the Examiner determined that "achieving ACR20 as early as 14 weeks after initiation of treatment is unexpected and surprising." *Id.*

These statements confirm that the Examiner expressly relied on the claimed clinical endpoints to distinguish the claims from the prior art. Those limitations are therefore "material to patentability and thus limiting." *See Allergan*, 935 F.3d at 1376 (citation omitted). Indeed, *Allergan* distinguished *Bristol-Myers*—the case on

which Petitioners rely (Pet. 37)—on precisely this ground. *Allergan*, 935 F.3d at 1376.

Petitioners' citation to the non-precedential *Baxter* and *Fresenius* decisions is also unavailing. Those cases involved situations where performing a single method step inevitably produced the claimed result—for example, administering a drug at a specific dosage interval necessarily minimized toxicity. *Baxter Healthcare Corp. v. Millenium Biologix, LLC*, IPR2013-00590, Paper 49 at 7-8, 10-11 (P.T.A.B. Mar. 18, 2015); *Fresenius-Kabi USA LLC v. Cubist Pharms., Inc.*, IPR2015-00227, Paper 13 at 5-7 (P.T.A.B. May 14, 2015).

Here, by contrast, achieving the claimed clinical endpoints depends on how the method is performed. Relevant choices include selecting a “safe and effective amount” of golimumab (*see* Ex.1003, 139:17), selecting appropriate co-administered medications in a “comprising” claim (*see id.* 3:55-56), selecting the “pharmaceutically acceptable carrier or diluent” (*see id.* 139:40-41), selecting the relevant patient population (*see id.* 87:57-93:16), and applying appropriate inclusion and exclusion criteria to obtain the claimed “mean change from baseline” and proportion of patients meeting clinical endpoints (*see id.* 139:47-48, 140:35-36). *See* Haroon ¶ 92. The claimed clinical endpoints are limiting because they determine whether those choices fall inside or outside the claims. *See Eli Lilly*, 8 F.4th at 1342.

The Federal Circuit in *Eli Lilly* distinguished Petitioners' authority, *Bristol-Myers*, on this same ground. *Id.* at 1342-43.

Finally, the claims themselves confirm that the clinical endpoints are limiting. Dependent claim 6, for example, refers to "said $\geq 65\%$ of patients that achieve ACR20 at week 14 of treatment." Ex.1003, 141:7-8. The clinical endpoint of independent claim 5 provides the antecedent basis for claim 6 and is therefore limiting. *Pacing Techs., LLC v. Garmin Int'l, Inc.*, 778 F.3d 1021, 1024 (Fed. Cir. 2015). Petitioners' contrary approach—stripping the clinical endpoints from the claims—would also render independent claims 1 and 3 verbatim identical, an outcome that is untenable under settled principles of claim construction. *Beachcombers Int'l, Inc. v. WildeWood Creative Prods. Inc.*, 31 F.3d 1154, 1162 (Fed. Cir. 1994) (claim construction that renders one claim superfluous to another is "presumptively unreasonable" (citations omitted)).

The claims at issue do not "simply require some general level of therapeutic effectiveness." *Allergan*, 935 F.3d at 1379 (Prost, C.J., concurring). Rather, they "specify clear and measurable metrics" for what must be achieved. *Id.* The claimed clinical endpoints should therefore be accorded full patentable weight.

VII. Petitioners Fail to Establish Prior Art Status of the Asserted References

The Petition must identify with particularity the grounds on which the challenge is based. 35 U.S.C. § 312(a)(3). This requirement includes identifying

the “supporting evidence relied upon to support the challenge.” 37 C.F.R. § 42.104(b)(5). Accordingly, the Petition must demonstrate that the asserted references qualify as prior art. “Thus, at the institution stage, the petition must identify, with particularity, evidence sufficient to establish a reasonable likelihood that the reference was publicly accessible before the critical date.” *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 at 13 (P.T.A.B. Dec. 20, 2019) (precedential). Petitioners bear the burden to make this showing. *Id.* at 16.

Public accessibility requires more than technical accessibility. Merely locating a document on a website, without more, cannot establish that it was publicly accessible. *See Samsung Elecs. Co. v. Infobridge Pte. Ltd.*, 929 F.3d 1363, 1369 (Fed. Cir. 2019); *Acceleration Bay, LLC v. Activision Blizzard Inc.*, 908 F.3d 765, 772-74 (Fed. Cir. 2018).

A. Petitioners Fail to Establish that NCT673-V23 Is Prior Art

NCT673-V23 is the linchpin of all three grounds in the Petition. Yet Petitioners fail to meet their burden to show that it qualifies as a printed publication as of the January 30, 2017 priority date.

To establish public accessibility, Petitioners assert that NCT673-V23 “was publicly available on ClinicalTrials.gov on January 8, 2016,” citing only the document itself and nearly duplicative statements by their expert to support that

alleged posting date. Pet. 22; Ex.1005 ¶ 161. These conclusory assertions are insufficient to establish a reasonable likelihood that it is prior art.

Exhibit 1011 (NCT673-V23) bears the date December 21, 2017, on its first page, far too late to qualify as prior art. Ex.1011, 1. The exhibit is a present-day capture of the clinical trial summary (NCT02181673) and does not show what information was available in 2016. Petitioners offer no corroborating evidence—such as a Wayback Machine capture or server logs—establishing that the portions of Exhibit 1011 purportedly corresponding to “version 23” were available in that form by January 8, 2016.

To the contrary, the Internet Archive's Wayback Machine indicates that it did not capture version 23 until after January 30, 2017. Ex.2059 (Wayback Machine Calendar of NCT673); *see also Valve Corp. v. Ironburg Inventions Ltd.*, 8 F.4th 1364, 1374 (Fed. Cir. 2021) (describing Wayback Machine). The absence of any archived version before the priority date, combined with Petitioners' lack of corroborating evidence, undercuts any suggestion that NCT673-V23 was “meaningfully indexed such that an interested artisan exercising reasonable diligence would have found it.” *See Samsung*, 929 F.3d at 1369 (original emphasis).

In an attempt to fill this gap, Petitioners' expert Dr. Fleischmann asserts that “a POSA searching for studies on ‘golimumab’ and ‘psoriatic arthritis’ would have readily found, among other studies, NCT02181673.” Ex.1005 ¶ 161. But Exhibit

1011 itself confirms that NCT02181673 has 33 versions, many of which are dated well after the priority date. Ex.1011, 2-3. Dr. Fleischmann does not verify which versions a POSA purportedly would have found before the priority date, much less establish that version 23 was among them. *See* 37 C.F.R. § 42.65(a); *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 at 15 (P.T.A.B. Aug. 24, 2022) (precedential) (declaration is entitled to little weight where it “adds little to the conclusory assertion for which it is offered to support”).

Dr. Fleischmann's reliance on the search function of ClinicalTrials.gov is misplaced because the search he “verified” was conducted using the present-day version of the website ClinicalTrials.Gov. Ex.1005 ¶ 161. But the search functionality available at the relevant time was far more limited. *Compare* Ex.2060 (Wayback Machine clinicaltrials.gov 2015), *with* Ex.2057 (Current clinicaltrials.gov 2026). Present-day search results do not establish what a POSA would have located using the search tools available before the priority date.

Finally, Petitioners rely on *Celltrion, Inc. v. Chugai*, for the proposition that ClinicalTrials.gov protocols are printed publications. IPR2022-00578, Paper 78 at 27-28 (P.T.A.B. Aug. 29, 2023). *Celltrion*, which is not precedential, cannot satisfy Petitioners' burden here. *Celltrion* does not hold that every clinical trial protocol on ClinicalTrials.gov automatically qualifies as a printed publication as of the date it bears. Rather, *Celltrion* turned on specific evidence of accessibility presented in that

case, including detailed testimony regarding an expert's search strategy to locate the particular publication in question—evidence that is absent here. *See id.* Paper 45 at 6-7 (Mar. 24, 2023).

Petitioners failed to address the *Hulu* standard at institution and therefore cannot carry their burden to show that NCT673-V23 qualified as a printed publication before the priority date. This failure is fatal to all three grounds in the Petition. The Director should not institute trial on Petitioners' deficient showing.

B. Petitioners Fail to Establish PI2013-Aria and PI2015-Simponi Are Prior Art Printed Publications

Petitioners likewise fail to carry their burden to show public accessibility of PI2013-Aria and PI2015-Simponi. Indeed, they offer no supporting evidence or argument. Instead, the Petition and Dr. Fleischmann rely exclusively on the labels' revision dates. Pet. 24-25; Ex.1005 ¶¶ 211, 220. That is not enough.

The Board squarely addressed this issue in *Mylan Pharmaceuticals Inc. v. Boehringer Ingelheim International GmbH*, IPR2016-01566, Paper 15 (P.T.A.B. Feb. 3, 2017). Like Petitioners here, the *Mylan* petitioners relied solely on the revision date to assert public availability. *Id.* at 11-12. And, as here, the petitioners' declarant failed to establish personal knowledge of the product label. *Id.* at 12. The Board explained that the label revision date does not satisfy petitioner's burden at the institution stage. *Id.*; *see also Mylan Pharms. Inc. v. Boehringer Ingelheim Int'l GmbH*, IPR2016-01565, Paper 17 at 20 (P.T.A.B. Feb. 9, 2017) ("a date merely

printed on a reference is not synonymous with a publication date” (citation omitted)). For the same reasons, institution based on PI2013-Aria and PI2015-Simponi should be denied.

C. Petitioners Should Not Be Permitted to Offer New Evidence in Reply

Petitioners were required to establish in the Petition a reasonable likelihood that the asserted references qualify as printed publications, but failed to do so. They may not cure that deficiency with new theories on reply. *See Intelligent Bio-Systems, Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016) (“Unlike district court litigation—where parties have greater freedom to revise and develop their arguments over time and in response to newly discovered material—the expedited nature of IPRs bring with it an obligation for petitioners to make their case in their petition to institute.”).

A reply requires a showing of good cause. 37 C.F.R. § 42.108(c). But good cause does not exist here because Petitioners’ prima facie case required sufficient evidence of public accessibility in the Petition itself. *Hulu*, IPR2018-01039, Paper 29 at 13. “Petitioner may not submit new evidence or argument in reply that it could have presented earlier, e.g. to make out a prima facie case of unpatentability.” USPTO, Patent Trial and Appeal Board Consolidated Trial Practice Guide at 73 (Nov. 2019), <https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf?MURL=TrialPracticeGuideConsolidated>.

VIII. Petitioners Fail to Establish a Reasonable Likelihood of Prevailing on Anticipation (Ground 1)

Anticipation is a demanding standard. *Eli Lilly & Co. v. L.A. Biomedical Rsch. Inst. at Harbor-UCLA Med. Ctr.*, 849 F.3d 1073, 1076 (Fed. Cir. 2017) (“*L.A. Biomedical*”). The prior art must disclose each and every claim limitation, not merely suggest it. *Id.* at 1074-75.

Anticipation by inherent disclosure applies “only when the reference discloses prior art that must *necessarily* include the unstated limitation.” *Transclean Corp. v. Bridgewood Servs., Inc.*, 290 F.3d 1364, 1373 (Fed. Cir. 2002) (original emphasis) (citation omitted). Inherency “may not be established by probabilities or possibilities.” *Rapoport v. Dement*, 254 F.3d 1053, 1063 (Fed. Cir. 2001).

A. NCT673-V23 Does Not Disclose “At Least One Pharmaceutically Acceptable Carrier or Diluent”

Independent claims 1 and 3 of the ’824 Patent require “at least one pharmaceutically acceptable carrier or diluent.” Ex.1003, 139:40-41 (claim 1), 140:29-30 (claim 3). Petitioners concede that “NCT673-V23 does not expressly state that the golimumab was dispersed in a pharmaceutically acceptable carrier or diluent as required by independent claims 1 and 4 [*sic*].” Pet. 43. That concession ends the anticipation inquiry because a reference cannot anticipate unless it discloses every claim limitation. *L.A. Biomedical*, 849 F.3d at 1074-75.

Petitioners seek to fill this gap by invoking the knowledge of a POSA. Pet. 44 (“a POSA would also know that the drug and placebo both have to be diluted”). This argument fails for two reasons.

First, the PTAB rules do not permit it. Petitioners were required to “specify where each element of the claim is found in the prior art patents or printed publications relied upon.” 37 C.F.R. § 42.104(b)(4). Petitioners cannot reach beyond those references to supply a missing limitation from the alleged knowledge of a POSA. As Acting Director, Coke Morgan Stewart recently explained, “expert testimony, common sense, and other evidence that is not ‘prior art consisting of patents or printed publications’ (collectively, ‘general knowledge’) may not be used to supply a missing claim limitation.” Ex.2033 (“7/31/2025 Acting Dir. Mem.”), 1.

Second, Petitioners improperly attempt to combine references under the guise of anticipation. The Petition asserts that a POSA allegedly would have known of the pharmaceutically acceptable carrier from PI2013-Aria. Pet. 44. Petitioners thus rely on PI2013-Aria to supply a limitation missing from NCT673-V23. That is not anticipation. “When more than one reference is required to establish unpatentability of the claimed invention anticipation under [35 U.S.C.] § 102 can not be found, and validity is determined in terms of [35 U.S.C.] § 103.” *Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1267 (Fed. Cir. 1991).

B. NCT673-V23 Does Not Disclose Administration “Over 30±10 Minutes”

Independent claims 1, 3, and 5 of the '824 Patent require that the anti-TNF α antibody is administered “over 30±10 minutes.” Ex.1003, 139:44 (claim 1), 140:32-33 (claim 3), 141:2-3 (claim 5). Petitioners concede “*NCT673-V23* does not expressly state that the golimumab was infused over a period of 30±10 minutes,” again improperly relying on the knowledge of a POSA and an additional different reference, PI2013-Aria, to supplant what *NCT673-V23* cannot show. Pet. 45; Haroon ¶ 96. For the same reasons stated above, Petitioners cannot rely on additional references to expand upon *NCT673-V23* under a theory of anticipation. *See supra* Section VIII.A.

C. NCT673-V23 Does Not Disclose the Claimed Clinical Endpoints

The independent claims of the '824 Patent require that treatment with golimumab achieve specific clinical endpoints:

- Claim 1: “at week 14 of treatment patients treated with the anti-TNF- α antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Health Assessment Questionnaire Disability Index score (HAQ-DI)= -0.60 ± 0.53 SD, enthesitis= -1.87 ± 1.75 SD, dactylitis= -7.8 ± 8.57 SD, Short-Form Health Survey Physical Summary score (SF-36 PCS)= 8.65 ± 7.60 SD, and Short-Form Health

Survey Mental Component Summary score (SF-36 MCS)= 5.33 ± 9.95 SD”
(Ex.1003, 139:45-55);

- Claim 3: “at week 24 of treatment patients treated with the anti-TNF- α antibody achieve a mean change from baseline in total modified van der Heijde-Sharp score (vdH-S)= -0.36 ± 0.144 SE” (*id.* 140:34-37);
- Claim 5: “ $\geq 65\%$ of patients receiving the treatment achieve ACR20 at week 14 of treatment” (*id.* 141:4-6).

NCT673-V23 discloses none of these claim limitations.

Petitioners attempt to overcome that deficiency through inherent anticipation. They rely on their expert's assessment that, because NCT673-V23 describes the same underlying clinical trial whose endpoints are reported in Example 9 of the '824 Patent, NCT673-V23 “should give the same results.” Ex.1005 ¶ 420. That theory is flawed for several reasons.

Inherent anticipation requires inevitability, not probability. *Rapoport*, 254 F.3d at 1063 (inherency “may not be established by probabilities or possibilities”). Dr. Fleischmann asserts that NCT673-V23's online summary—as briefly described across three pages excluding version numbers and study location—“should give” the same results. Ex.1005 ¶ 420. But the data shows that the achievement of the claimed clinical endpoints is not inevitable. *See* Haroon ¶ 98.

Thus, there is no anticipation because the claimed clinical endpoint is not *necessarily* present. *See Transclean*, 290 F.3d at 1373.

Apotex Inc. v. Regeneron Pharmaceuticals, Inc., is directly on point. IPR2022-01524, Paper 9 (P.T.A.B. Mar. 10, 2023). In *Apotex*, the challenger relied on a clinical trial protocol to challenge claims that required that “the patient achieves a gain in visual acuity within 52 weeks.” *Id.* at 7, 25-26. As here, the challenger asserted that the results should be the same because the protocol described the same study as Example 4 of the patent. *Id.* at 26.

The Board in *Apotex* rejected the inherent anticipation argument. It explained that “the evidence shows that the claimed *results limitations* may *typically* flow from the claimed method, but not *necessarily*.” *Id.* at 34 (original emphases). NCT673-V23 would not necessarily achieve the same claimed clinical endpoints because it does not disclose the same patient population in which the '824 Patent achieved those endpoints. Haroon ¶¶ 64-78, 100-103. The omission of those patient-selection criteria could affect treatment outcomes and yield materially different clinical endpoints from those reported in the '824 Patent. *Id.*

The specification of the '824 Patent requires the study population to meet certain criteria, including CASPAR, PsA subsets, and concurrent treatments. *Id.* ¶¶ 66-74. It also articulates important aspects of its study design, including efficacy

analysis and early escape methods. *Id.* ¶¶ 75-77. In contrast, NCT673-V23 is silent with respect to these key criteria. *Id.* ¶¶ 64-78.

The specification of the '824 Patent requires a study population that meets classification criteria for PsA ("CASPAR"). Ex.1003, 77:55-58, 86:4-7, 88:14-16. CASPAR is a high-specificity diagnostic tool for PsA patients with component measures in psoriasis, psoriatic nail dystrophy, rheumatoid-factor negativity, dactylitis, and radiological evidence of new bone formation. Haroon ¶ 66.

NCT673-V23 does not disclose this inclusion criteria. *Id.* ¶ 67. Instead, at the time of the invention, a POSA could have applied a different PsA classification tool or opted for no classification requirements. *Id.* For example, other clinical trials at the time employed the Moll & Wright symptomatic disease definition. *Id.*; see Ex.2092 (Schett 2012), 3157. Those differences would materially affect the patient population enrolled in the study and, in turn, change the resulting efficacy of the claimed clinical endpoints. Haroon ¶ 67; Ex.2094 (Taylor 2006), 2666.

The '824 Patent specification states that the patient population must have one of the PsA subsets, such as arthritis mutilans (i.e., severe joint inflammation and damage). Ex.1003, 88:22-25. NCT673-V23 does not provide this information. Dr. Haroon explains that the definition of and threshold for arthritis mutilans varies across studies. Haroon ¶¶ 68-69. Subjects with arthritis mutilans are particularly

difficult to treat because their irreversible, advanced disease state limits the likelihood of improvement to clinical endpoints, including HAQ-DI. *Id.*

Further, the '824 Patent specification requires the study's efficacy analysis be based on an intent-to-treat analysis, which includes all randomized subjects regardless of protocol adherence, or how its early escape is conducted. *See* Ex.1003, 80:29-34. NCT673-V23 is silent on the type of efficacy analysis required. At the priority date, other analytical approaches were common, including per-protocol analysis that considered only subjects who adhered to the protocol. Haroon ¶¶ 75-77. These differing methodologies can produce different clinical efficacy outcomes. *Id.*; Ex.2063 (Bai 2021), Abstract.

Because NCT673-V23 omits parameters that can significantly affect the resulting clinical trial endpoints, it does not anticipate the claims because it would not “necessarily” achieve the same claimed clinical endpoints. *Transclean*, 290 F.3d at 1373.

There can be no inherent anticipation of efficacy outcomes when the prior art involves different patient populations, as the Board held in *Apotex*. IPR2022-01524, Paper 9 at 36-38. In that case, the prior art clinical trial protocol differed from the challenged patent because it lacked exclusion criteria for certain conditions such as uveitis, which were excluded in the patent. *Id.* at 36-37. In *Apotex*, as here (*see* Haroon ¶¶ 100-103), there was “evidence of potential variance in results based on

patients generally and patient populations specifically, which negates the inherency of the *results limitations*.” *Apotex*, IPR2022-01524, Paper 9 at 37 (original emphasis). Because different patient populations can yield different clinical efficacy outcomes, the claimed clinical endpoints are not inherently disclosed. *Id.*

IX. Petitioners Fail to Establish a Reasonable Likelihood of Prevailing on Obviousness Over NCT673-V23 and PI2013-Aria (Ground 2)

In Ground 2, Petitioners seek to combine NCT673-V23 with the label for IV administration of golimumab to treat RA (PI2013-Aria). That combination fares no better than NCT673-V23 alone.⁴

Petitioners concede that “neither NCT673-V23 nor PI2013-Aria disclose the claimed clinical outcomes.” Pet. 51. And, as discussed above, NCT673-V23 does not inherently disclose the claimed clinical endpoints. *See supra* Section VIII.C. Because “an obviousness determination generally requires a finding that ‘all claimed limitations are disclosed in the prior art’” (*Univ. of Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 160 (Fed. Cir. 2021) (citations omitted)), Petitioners’ failure to show that the prior art discloses the claimed clinical endpoints is fatal to Ground 2.

Under Rule 104(b)(4), Petitioners may not rely on the knowledge of a POSA to supply a missing claim limitation. The rule requires Petitioners to “specify where

⁴ As a threshold matter, Petitioners failed to show these references were prior art. *See supra* Section VII.

each element of the claim is found in the prior art patents or printed publications relied upon” (37 C.F.R. § 42.104(b)(4)), not how the limitation might be derived from general knowledge or other non-prior-art sources. *See* 7/31/2025 Acting Dir. Mem., 1 (“evidence that is not ‘prior art consisting of patents or printed publications’ ... may not be used to supply a missing claim limitation”); *see also* 35 U.S.C. § 311(b).

Because NCT673-V23 and PI2013-Aria fail to disclose all limitations of the challenged claims even when considered together, Petitioners cannot establish either a motivation to combine the references to arrive at the claimed invention or a reasonable expectation of success in achieving what is claimed. Motivation to combine and reasonable expectation of success must be measured against the specific invention as claimed, not a generic objective. *See Janssen Pharms., Inc. v. Teva Pharms. USA, Inc.*, 141 F.4th 1367, 1379-80 (Fed. Cir. 2025) (“[i]t is bedrock law that the inquiry of motivation and reasonable expectation of success must focus on arriving at the *claimed* invention” (original emphasis)). Where, as here, the proposed combination omits entire claim limitations, Petitioners cannot show that a POSA would have been motivated to combine the references to arrive at the claimed invention, much less that the resulting combination would have been reasonably expected to achieve the claimed clinical endpoints.

The Petition provides no reason to second-guess the Examiner's determination that the combination of references would not have predicted the "unexpected and surprising" results in treating active PsA to achieve the claimed clinical endpoints. Ex.2002, -153-54.

X. Petitioners Fail to Establish a Reasonable Likelihood of Prevailing on Obviousness Over NCT673-V23, PI2013-Aria, PI2015-Simponi, GO-REVEAL, and WO213 (Ground 3)

It is telling that Petitioners must rely on eight references to try to reconstruct the patent claims. Even with that patchwork approach, the prior art still fails to disclose all claim limitations.

Ground 3 fails for at least three reasons: (1) even taken together, the eight prior art references (NCT673-V23, PI2013-Aria, PI2015-Simponi, GO-REVEAL, and WO213) do not disclose all claim limitations; (2) there would have been no motivation to combine the eight references in the manner proposed; and (3) there was no reasonable expectation of success.

A. NCT673-V23, PI2013-Aria, PI2015-Simponi, GO-REVEAL, and WO213 Do Not Disclose the Claimed Clinical Endpoints

Petitioners admit that NCT673-V23 and PI2013-Aria do not disclose the claimed clinical endpoints. Pet. 51 ("neither NCT673-V23 nor PI2013-Aria disclose the claimed clinical outcomes"). The remaining three references, all of which concern SC administration of golimumab or adalimumab, likewise fail to disclose the claimed clinical endpoints.

Independent claim 1 requires (among other endpoints) achieving HAQ-DI= -0.60 ± 0.53 SD change from baseline at week 14 of treatment. Ex.1003, 139:45-55. Petitioners rely on Kavanaugh 2009 for its disclosure of HAQ-DI scores of 0.33 ± 0.55 and 0.39 ± 0.50 at week 24. *See* Pet. 54-55. Petitioners also rely on WO213 for its disclosure of HAQ-DI score -0.3 ± 0.5 SD at week 24. *Id.* 56. Claim 1 expressly recites both the mean (-0.60) and the standard deviation (± 0.53); both therefore form part of the claim limitation. Setting aside the different route of administration, Kavanaugh 2009 and WO213 fail on both fronts: all of the reported mean values are smaller (worse) and several standard deviations are also broader (worse) than those recited in the claim. Nor does Kavanaugh 2009 report the HAQ-DI endpoint at the claimed week 14 timepoint. Haroon ¶ 107. This claim limitation is therefore absent from the asserted prior art, and Petitioners may not rely on expert testimony to supply the missing claim limitation. 7/31/2025 Acting Dir. Mem., 1.

Nor would a POSA have reasonably expected the claimed IV administration of golimumab to achieve such dramatically faster clinical endpoints, particularly in light of contemporaneous studies reporting lower efficacy with IV administration than with SC administration. Rutgeerts 2015, 504; *see also* Haroon ¶ 107; *supra* Section II.D. In any event, even if such speculation had merit, it cannot substitute for disclosure of a claim limitation that is missing from the asserted prior art patents

and printed publications. 7/31/2025 Acting Dir. Mem., 1 (expert testimony “may not be used to supply a missing claim limitation”).

Independent claim 3 requires achieving total modified vdH-S= -0.36 ± 0.144 SE at week 24 of treatment. Ex.1003, 140:34-37. Petitioners rely on Kavanaugh 2012 for its disclosure of total modified vdH-S scores 0.34 ± 1.10 and 0.16 ± 1.36 at week 24. Ex.1042, 2509; Pet. 59. Petitioners also rely on WO213 for its disclosure of total modified vdH-S score -0.2. Ex.1025, 127-28; *see* Pet. 60. Yet, WO213 reports the clinical endpoints of a different biologic (adalimumab), not golimumab. The mean total modified vdH-S scores reported by Kavanaugh 2012 and WO213 are worse than the claimed clinical endpoint. Again, claim 3 expressly recites both the mean (-0.36) and the standard error (± 0.144); both therefore form part of the claim limitation. Unlike the '824 Patent, which provides a standard error value, Kavanaugh 2012 reports a standard deviation. Haroon ¶¶ 115-116. Thus, Kavanaugh 2012 and WO213 disclose worse means and no standard error. Petitioners may not rely on expert testimony to supply the missing claim limitation. 7/31/2025 Acting Dir. Mem., 1.

Independent claim 5 requires that $\geq 65\%$ of patients achieve ACR20 at week 14 of treatment. Ex.1003, 141:4-6. Petitioners again rely on Kavanaugh 2009 for its disclosure that 51% of patients achieved ACR20 at week 14. Ex.1041, 979; Pet. 62. This value falls below the claimed threshold of $\geq 65\%$, and thus the claim

limitation is not disclosed. Haroon ¶ 119. Petitioners also rely on WO213 for its disclosure that 72% of patients achieved ACR20 at week 12 of treatment with adalimumab. Pet. 62. However, this data is the result of a different therapy and route of administration, at a different timepoint, in an open-label practice (not a randomized controlled trial). Haroon ¶ 120. Petitioners again would need to rely on expert testimony to bridge these significant gaps between the reference and the patented invention. Thus, Petitioners' arguments are insufficient.

Petitioners attempt to dismiss these deficiencies as "small differences." Pet. 60. But "proximity alone is not enough to establish a prima facie case of obviousness," and it is error to rely on small differences to establish a prima facie case of obviousness. *In re Patel*, 566 F. App'x 1005, 1010 (Fed. Cir. 2014). "Close enough" is not a permissible substitute for an actual disclosure in the prior art. 7/31/2025 Acting Dir. Mem., 1.

B. Petitioners Fail to Establish a Motivation to Combine

It is not enough to identify claim limitations in the prior art—and here, Petitioners have not even done that. There also must be a motivation to combine the prior art teachings to arrive at the claimed invention. *Virtek Vision Int'l ULC v. Assembly Guidance Sys., Inc.*, 97 F.4th 882, 887-88 (Fed. Cir. 2024).

The first step of Petitioners' eight-reference combination is to combine NCT673-V23 (directed to treatment of PsA) with PI2013-Aria (directed to treatment

of RA). Petitioners' theory fails at the outset. These references concern different diseases with distinct pathologies, in different patient populations. *See supra* Section II.B. A POSA would have understood that PsA and RA require materially different treatment approaches. *See supra* Section II.C. Notably, Petitioners have not even attempted to argue motivation or expectation to obtain the claimed invention in connection with Ground 2.

Petitioners claim that NCT673-V23 can be combined with PI2013-Aria because both are "used for the same purpose—to treat a TNF- α related disease in humans." Pet. 49. This broad generalization fails because TNF plays materially different roles in each disease. Haroon ¶¶ 33-40; *see also supra* Section II.B.

Petitioners' argument that the references should be combined because they "are both Janssen publications" (Pet. 49), fares no better. The Board has rejected such a hindsight-driven rationale: "We are not persuaded that the close ownership relationship [between two references] would prompt the person of ordinary skill to make the proposed combination." *VMWare, Inc. v. Elecs. & Telecomms. Rsch. Inst.*, IPR2014-00901, Paper 35 at 30 (P.T.A.B. Dec. 9, 2015).

After NCT673-V23 and PI2013-Aria, Petitioners next try to add PI2015-Simponi, GO-REVEAL, and WO213 to the combination, claiming they would be combined because they "all concern the efficacy of golimumab and equivalent anti-TNF α antibody treatments." Pet. 58. But those three references disclose only SC

administration of golimumab, not the claimed IV administration. Haroon ¶¶ 128-129. A POSA would have had no reason to combine references directed to fundamentally different routes of administration. *See supra* Section II.D. To the contrary, the POSA would have understood that SC and IV golimumab were “separate and distinct products” with “different pharmacokinetic characteristics, dosing regimens, and product presentations.” Ex.1034, 127. Petitioners’ asserted motivation to combine is untethered to the realities of the art at the time.

C. Petitioners Fail to Establish a Reasonable Expectation of Success

Petitioners must show that a POSA would have had a “reasonable expectation of successfully achieving the claimed invention from the combination.” *Eli Lilly*, 8 F.4th at 1344 (citations omitted). Petitioners argue that a POSA would have had a reasonable expectation of success based on prior use of golimumab in a different formulation (SC) for a distinct disease (RA). Pet. 54, 60-61, 62-63. Petitioners fail to meet their burden.

1. A POSA Would Not Have Reasonably Expected to Achieve the Claimed Clinical Endpoints Based on the Prior Art

Petitioners rely on studies of SC golimumab or adalimumab (PI2015-Simponi, GO-REVEAL, WO213) and IV golimumab for a different disease (PI2013-Aria), together with nothing more than a protocol proposing to study IV golimumab in PsA (NCT673-V23). The references discuss data that resulted from a different therapy

or via a different route of administration. Such evidence cannot support a reasonable expectation of success.

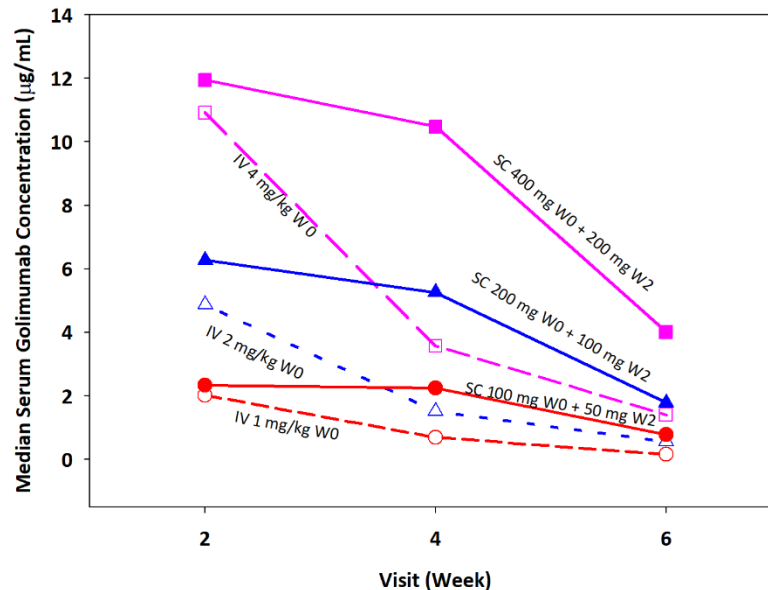
The SC golimumab efficacy data in the prior art fail to disclose the claimed clinical endpoints. *See supra* Section X.A. Petitioners do not appear to dispute this. *See, e.g.*, Pet. 60. Instead, Petitioners argue that the claimed clinical endpoints would have been obvious because of “the higher drug exposure of the IV versus SC formulation.” *Id.*; *see also id.* 55, 63.

Petitioners’ bioavailability argument conflicts with the scientific understanding of a POSA at the time, who would have understood there to be no dose response, i.e., a POSA would not necessarily expect a higher golimumab dose to have a higher efficacy. A contemporaneous study of IV golimumab in UC reported that “no dose-response was observed.” Rutgeerts 2015, 512. The study also stated that “peak serum golimumab concentration [$C_{\max}$] is not a dominant driver of efficacy.” *Id.* 511. In other words, a POSA at the time of the invention understood that more drug did not translate into improved clinical outcomes, so a POSA could not have expected the claimed clinical endpoints. Haroon ¶ 137.

Furthermore, IV administration did not necessarily result in higher bioavailability. In Rutgeerts 2015 (Ex.2089), the investigators measured serum golimumab concentrations for IV and SC dosage regimens that “were expected to provide comparable systemic drug exposure.” Rutgeerts 2015, 509-10. The study

included three head-to-head comparisons between IV and SC administration, as shown in Figure S2 of the Supplemental Appendix ("Rutgeerts App'x," Ex.2090):

Figure S2. Median Serum Golimumab Concentration by Study Visit (Week) and by Induction Dose and Regimen



PURSUIT-IV (dashed lines, open symbols); PURSUIT-SC (solid lines, solid symbols)

Rutgeerts App'x, 13. For each matched pair (magenta, blue, red), the IV administration (dashed line) produced lower blood levels that declined more rapidly than those observed with SC administration (solid line). *Id.* In each comparison, contrary to Petitioners' obviousness theory, the IV administration did not result in higher bioavailability. Haroon ¶¶ 131-133. Thus, the asserted references would have failed to provide a POSA with a reasonable expectation of success.

To the extent SC efficacy data have any relevance to the claims, they further undermine Petitioners' bioavailability theory. The prior art, including Kavanaugh 2012 and other contemporaneous references, shows a plateau effect for SC

golimumab efficacy from 50 mg to 100 mg at certain endpoints. *See, e.g.*, Ex.1016 (Inman), 3406 (Figs. 2-3); Ex.1033 (van der Heijde 2014), 1099 (Fig. 1); Ex.1042, 2513 (Fig. 3). PI2015-Simponi likewise states that there was “no clear evidence of improved ACR response with the higher SIMPONI dose group (100 mg) compared to the lower SIMPONI dose group (50 mg).” Ex.1015, 26. This plateau effect conflicts with Petitioners’ theory that increased bioavailability would necessarily produce superior clinical efficacy relative to existing dosage regimens, which undermines any reasonable expectation of success. Haroon ¶ 137.

2. The Failure of IV Golimumab for UC Negates Any Reasonable Expectation of Success

Before the invention, Janssen had attempted to transition golimumab from SC administration to IV administration to treat UC. But IV administration proved unsuccessful. Haroon ¶ 132. That failure underscores the absence of any reasonable expectation of success here.

The PURSUIT-IV trial compared SC and IV golimumab to treat UC. Rutgeerts 2015. The investigators selected doses that “were expected to provide comparable systemic drug exposure.” *Id.* 509-10. Efficacy was measured based on clinical response and clinical remission. *Id.* 505. The data showed that IV administration offered no benefit over SC administration:

The profile following two SC administrations of golimumab thus appeared more favourable for clinical efficacy than that following IV administration of a single golimumab dose.... In summary, single-dose IV administration of golimumab in patients with moderate-to-severe UC did not lead to significant improvement in clinical outcome[.]

Id. 511-12. Based on this unsuccessful result, the study was terminated. Ex.2058, 1 (“Protocol was cancelled by company based on overall efficacy”).

At the time this UC study was terminated, SC golimumab was approved and routinely used to treat UC. Ex.1015, 1. But after this unsuccessful effort, IV golimumab was never approved for UC. Haroon ¶ 131. That failure illustrates why prior success with SC golimumab cannot create a reasonable expectation of success for IV golimumab. Thus, there was no reasonable expectation of success at the time of the invention.

3. The FDA Record on IV Golimumab for RA Negates Any Reasonable Expectation of Success

The FDA's contemporaneous views provide a reasonable proxy for the perspective of a POSA at the time of the invention. Haroon ¶¶ 135-136. By the priority date, the FDA concluded that clinical data for SC administration of golimumab for RA could not be extrapolated to IV administration. *Id.*

SC golimumab was approved to treat RA in 2009. Ex.1034, 233. By 2011, Janssen was developing an IV golimumab for RA and planned to seek FDA approval

for that product. *Id.* 126. In support of its application, Janssen proposed relying, in part, on “data from different SC dose regimens in patients with RA.” *Id.* 127.

The FDA rejected that premise. As the agency explained, it “consider[s] the IV and SC formulations of golimumab to be two separate and distinct products because they have different pharmacokinetic characteristics, dosing regimens, and product presentations, despite having the same drug substance.” *Id.* The FDA further warned that, “[g]iven the differences of the IV and SC regimens, you will need to provide evidence of independent substantiation of the efficacy of IV golimumab.” *Id.*

The FDA specifically cautioned that “it may not be possible to extrapolate efficacy data from the SC golimumab RA program” because IV administration may result in lower trough blood levels of golimumab compared to SC administration. *Id.* 128-29. These contemporaneous FDA statements confirm that a POSA would not have reasonably expected the clinical efficacy observed with SC administration of golimumab to translate to IV administration. Haroon ¶¶ 135-136.

XI. Conclusion

For the reasons set forth above, the Board should deny the Petition for Inter Partes Review.

Respectfully submitted,

Dated: June 29, 2026

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CERTIFICATE OF COMPLIANCE WITH 37 C.F.R. § 42.24

I hereby certify that this Patent Owner's Preliminary Response complies with the word count limitation of 37 C.F.R. § 42.24(b)(1) because the Patent Owner's Preliminary Response contains 12,100 words using Microsoft Word's counting feature, excluding the cover page, signature block, and the parts of the Patent Owner's Preliminary Response exempted by 37 C.F.R. § 42.24(b)(1).

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I certify that on this 29th day of June, 2026, a true and correct copy of the foregoing **Patent Owner's Preliminary Response and all Exhibits** were served by electronic mail on Petitioners' lead and backup counsel at the following email addresses:

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