

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.

IPR2026-00259
Patent No. 12,291,566

**PATENT OWNER'S
PRELIMINARY RESPONSE**

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TABLE OF ABBREVIATIONS**Medical terms**

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

Clinical endpoints and indices

ASAS	Assessment in Ankylosing Spondylitis
ASDAS	Ankylosing Spondylitis Disease Activity Score
ASQoL	Ankylosing Spondylitis Quality of Life Questionnaire
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
BASMI	Bath Ankylosing Spondylitis Metrology Index
SF-36 MCS	Short-Form Health Survey Mental Component Summary
SF-36 PCS	Short-Form Health Survey Physical Component Summary
VAS	Visual Analogue Scale

EXHIBIT LIST

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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. 12,291,566 (“the ’566 Patent”). The ’566 Patent claims methods for treating active ankylosing spondylitis (“AS”) 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 NCT873-V24 (Ex.1014), an online summary of a clinical trial protocol. Although the document states “Viewing V24 (2015-10-27),” it bears a “Last Update” date in 2025. *Id.* 4. That notation does not satisfy Petitioners’ burden to establish NCT873-V24 as prior art. The record contains no evidence that the purported “V24” content was publicly accessible on October 27, 2015. Nor do Petitioners show (assuming it was available online) that V24 was meaningfully indexed so a POSA would have found it.

But even if NCT873-V24 were prior art—and it is not—Petitioners’ challenge still fails because NCT873-V24 does not disclose the claimed clinical endpoints recited in the ’566 Patent. Further, NCT873-V24 not only omits key criteria defining the relevant patient population, it affirmatively states that additional, unspecified

inclusion and exclusion criteria applied. Petitioners resort to inherent anticipation to supply the missing limitations but fail to demonstrate that the missing limitations are necessarily present in NCT873-V24. 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 AS "differ substantially" such that their treatments "should therefore also differ." Ex.2096, 1 (Schett 2011). 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 have not shown a reasonable likelihood of prevailing on any challenged claim, Janssen respectfully requests that the Director deny institution.

II. Background

A. Ankylosing Spondylitis

AS is a chronic inflammatory disease of unknown etiology that affects the joints, including the spine, entheses (where connective tissue attaches to bone), and peripheral joints. Ex.1004, 84:47-50. AS may lead to substantial loss of mobility and disability, significantly impairing patients’ quality of life and functional capacity. *Id.* 84:54-58. AS belongs to the family of diseases called spondyloarthritis (“SpA”). Ex.2054 (“Haroon”) ¶ 35.

Patients with AS often have elevated TNF levels. *Id.* 85:12-16. But as Petitioners acknowledge, “the precise role of TNF α in AS is not fully understood.” Pet. 6. In particular, the degree to which TNF inhibition would ameliorate the full spectrum of AS manifestations remained uncertain ahead of the priority date. *See, e.g.,* Ex.2072, 1452 (Baraliakos 2007).

Clinicians assess AS treatment success using validated, disease-specific clinical endpoints. Haroon ¶¶ 26-34. They include:

- Ankylosing Spondylitis Disease Activity Score (ASDAS): a composite score incorporating patient-reported items and an objective measurement such as C-reactive protein (“CRP”) levels;
- Assessment in Ankylosing Spondylitis (ASAS): a composite improvement measure across four domains: patient global assessment, pain, function, and inflammation;
- Bath Ankylosing Spondylitis Functional Index (BASFI): a patient self-assessment tool measuring functional limitations in daily activities;
- Bath Ankylosing Spondylitis Metrology Index (BASMI): a standardized clinical tool used to measure spinal mobility and movement limitations;
- Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL): a disease-specific quality of life questionnaire;
- 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.

Id. ASDAS, ASAS, BASFI, BASMI, and ASQoL are clinical endpoints specific to AS and have not been validated for use in RA. *Id.* ¶ 28.

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

Petitioners' invalidity arguments rest on a superficial comparison between RA and AS. *See, e.g.*, Pet. 15-16 ("Like RA, patients with AS have impaired physical function and health-related quality of life."). But a POSA would have understood that RA and AS are distinct diseases with materially different biology and clinical characteristics.

RA and AS 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 ¶ 40. 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.* AS, 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.2083, S-12 (Lories 2009) ("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 AS, TNF is associated with macrophages and mast cells. Haroon ¶ 40.

The immunological differences are also reflected in whether patients have rheumatoid factor antibodies in their blood. Haroon ¶ 25. Patients with RA typically test positive for rheumatoid factor. *Id.* ¶¶ 25, 36. 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 AS and psoriatic arthritis (“PsA”). *Id.*

The genetic underpinnings of the two diseases are also distinct. By the priority date, AS was strongly associated with the genetic marker HLA-B27, while RA was associated with different markers: HLA-DR1 and -DR4. Ex.2076 (Ghasemi-rad 2015), 238-39; Ex.2123 (Fugger & Svejgaard 2000), Abstract. There is “little overlap between factors affecting susceptibility to the two diseases.” Ex.2085 (Maksymowych 2009), S-24.

RA and AS also affect different tissues. In RA, inflammation occurs primarily in synovial tissue and peripheral joints, and axial involvement is rare. Ex.2083, S-10-11 (Lories 2009). AS, by contrast, predominantly affects axial joints (i.e., the spine) and entheses (sites where tendons or ligaments meet bone), and may also manifest in the skin. *Id.*

RA and AS patient populations also differ markedly. RA predominantly affects female patients, whereas AS predominantly affects male patients. Ex.2093, 99 (Rugiene 2008); Ex.2114, 2 (Vollenhoven 2009). RA typically presents later in life, while AS often begins during adolescence or early adulthood. Ex.2074, 12, 14 (Elyan 2006).

Petitioners and their expert largely ignore these critical distinctions between AS and RA, offering only a superficial overview of each disease. *See* Pet. 14-15; Ex.1005 ¶¶ 44-46. That omission is significant. The fundamental differences between AS and RA directly shape the treatment strategies and therapeutic options available for each disease. *See* Haroon ¶¶ 44-52.

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

A POSA would have understood that the differences between RA and AS also extended to treatment. For example, at the priority date, a POSA would have known that RA patients required methotrexate (“MTX”) with Simponi, whereas the same is not true for AS patients. Haroon ¶ 52.

A POSA at the time of the invention likewise understood that AS 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 AS required—and continue to require—different therapeutic approaches. For instance, a POSA would have recognized that tocilizumab (“TCZ”) was approved for RA but failed as

a treatment for AS. *See* Ex.2098, 95, 99 (Sieper 2014) (“TCZ is not an effective treatment for patients with AS.”). Further, even among anti-TNF agents, efficacy and dosing differed at the time of the claimed invention, and are still different today. For example, infliximab requires higher and more frequent dosing in AS than in RA. *See* Ex.2068 (REMICADE® (infliximab) Label). The contemporaneous literature explained that because RA and AS “differ substantially in their patterns of bone and cartilage damage.... Goals and strategies to prevent and treat structural damage should therefore also differ.” Ex.2096, 1 (Schett 2011); *see also* Ex.2072, 1452 (Baraliakos 2007) (“It seems clear now that, in contrast to RA ... there is some radiographic progression in patients with AS over 2 and 4 yrs of anti-TNF therapy.”).

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 ¶¶ 56-63. 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.*

¶ 61. 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 ¶ 57. 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, 6 (EMA Withdrawal Assessment). 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 ¶ 61; Ex.2090, 332 (Naganuma) (“[S]ubcutaneous 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.2094 (“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 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

¶ 62. Experience with SC administration did not translate to IV, and efforts to bridge that gap were abandoned. Ex.2075, 882 (Flamant) (“[T]he proportion of patients achieving clinical response was low and studies with intravenous golimumab administration were not subsequently continued.”); Ex.2058 (“Protocol was cancelled by company based on overall efficacy”); *see also* Ex.2103, 410-11 (Steiner); Ex.2090, 332 (Naganuma); Ex.2106, 244 (Ungar).

III. The Asserted References

A. NCT873-V24 (Ex.1014)

NCT873-V24 is an online summary of a clinical trial protocol investigating IV golimumab in AS patients. Ex.1014. Aside from version information and study locations, its substantive disclosure spans just five pages. *Id.* As discussed below, Petitioners failed to establish that NCT873-V24 qualifies as prior art. *See infra* Section VII.A.

NCT873-V24 contains no data regarding the claimed clinical endpoints. Ex.1014. It discloses only the existence of an ongoing clinical trial, omitting key aspects of the protocol and instead referring to unspecified “additional protocol-defined” inclusion and exclusion criteria. *Id.* 9-10. NCT873-V24 does not disclose those additional criteria.

Compared with the ’566 Patent, NCT873-V24 fails to disclose key clinical trial parameters, including:

- Definition of “active ankylosing spondylitis” (Ex.1004, 79:58-65, 88:48-53, 89:51-54);
- Eligibility criteria for “active disease” as evidenced by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥ 4 and Visual Analogue Scale (VAS) ≥ 4 (*id.* 79:59-65, 88:48-53, 89:51-54);
- Inclusion of subjects with complete ankylosis of the spine, defined as bridging syndesmophytes present at all intervertebral levels of the cervical and lumbar spine (*id.* 88:66-89:4, 105:40-43);
- Inclusion of up to 20% of subjects with prior exposure to one TNF inhibitor (*id.* 88:62-65, 105:40-43);
- Efficacy calculation based on an intent-to-treat analysis (*id.* 82:25-30, 103:18-23).

Petitioners also concede that “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 3,” nor does it “expressly state that the golimumab was administered over 30 ± 10 minutes.” Pet. 41, 42.

Petitioners incorrectly assert that the “claims issued only because Janssen failed to disclose NCT873-V24 to the examiner.” Pet. 1. In fact, NCT873-V24 is cumulative of Wong (Ex.1024) and Zhuang (Ex.1038). *See* Paper 11 at 14-15. Wong is a U.S. patent application publication that describes a Phase III clinical study

of adalimumab to treat AS. Ex.1024. Zhuang is a 2012 publication reporting the PK profile of SC and IV golimumab in RA patients. Ex.1038. The Examiner concluded that Wong and Zhuang disclosed administering 2 mg/kg IV golimumab over 30 minutes, exactly what Petitioners allege here. *See* Paper 11 at 14-15.

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 ¶ 82. Instead, it reports inferior ASAS20 endpoints both before and after the 16-week mark recited in the '566 Patent claims. *Compare* Ex.1015, 29 (Table 6), *with* Ex.1004, 134:18-20 (independent claim 5). Nor does it disclose other claimed clinical endpoints, including ASDAS, BASMI, SF-36 MCS, SF-36 PCS, and ASQoL.

Other references expressly considered by the Examiner, including Inman and van der Heijde, disclose substantially the same thing as PI2015-Simponi. *See* Ex. 2002, -017, -022. Both concern SC administration of golimumab for AS, and Inman Figures 2 and 3 present the same ASAS20 data reported in PI2015-Simponi. *Compare* Ex.1015, 29-30 (Table 6 & Fig. 3), *with* Ex.1016, 3406 (Figs. 2-3). The

Examiner considered and allowed the claims over these references. Ex.2002, -017, -022, -383-84.

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 AS or the claimed clinical endpoints for AS. It is directed exclusively to RA, a disease understood to have a different pathology from AS and to require a different treatment strategy. *See supra* Sections II.B-C. A POSA would have recognized that RA and AS “differ substantially in their patterns of bone and cartilage damage,” and “[g]oals and strategies to prevent and treat structural damage should therefore also differ.” Ex.2096, 1 (Schett 2011).

D. Inman (Ex.1016)

Inman describes a clinical trial of SC golimumab to treat AS. It does not disclose IV administration of golimumab. Haroon ¶ 85. Inman also fails to disclose numerous clinical endpoints as recited in the claims. *Id.* ¶¶ 119-23. For ASAS20, Inman reports SC administration endpoints that are inferior to those claimed in the '566 Patent for IV administration. *Id.* ¶ 120; *compare* Ex.1016, 3402 (Abstract), *with* Ex.1004, 134:18-20 (independent claim 5). The Examiner considered Inman during prosecution of the '566 Patent. *See* Ex.2002, -017 (IDS).

E. Van der Heijde (Ex.1033)

Van der Heijde likewise describes a clinical trial of SC golimumab to treat AS, but it does not disclose IV administration of golimumab. Haroon ¶ 88. Van der Heijde also fails to disclose numerous clinical endpoints at the timepoints recited in the claims. *Id.* ¶¶ 109-16. With respect to ASDAS, van der Heijde reports outcomes at weeks 14 and 24, yet even after that extended treatment period, the ASDAS scores remain inferior (i.e., higher) to those achieved in the '566 Patent after just 2 or 4 weeks of IV golimumab treatment. *Id.* ¶¶ 110-11; *compare* Ex.1033, 1098 (Table 2), *with* Ex.1004, 131:63-67 (independent claim 1). The Examiner considered van der Heijde during prosecution of the '566 Patent. *See* Ex.2002, -022.

IV. The Patented Invention

The '566 Patent, titled “Anti-TNF Antibodies, Compositions, and Methods for the Treatment of Active Ankylosing Spondylitis,” 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 Ankylosing Spondylitis (AS).” Ex.1004 (Abstract). SEQ ID NOS: 36 and 37 correspond to golimumab. *Id.* 79:4-5.

The '566 Patent describes a multicenter, randomized, double-blind, placebo-controlled clinical trial of IV golimumab to treat AS. *Id.* 78:60-110:46. The study showed marked improvement in AS across multiple clinical endpoints. For

example, patients achieved significant clinical endpoints as early as week 2 or 4 (< 1.3 ASDAS) and at week 16 ($\geq 65\%$ achieving ASAS20). *Id.* 106:25-107:35 (Tables 8-9).

The priority date of the '566 Patent is February 7, 2017, *see id.* (Related U.S. Application Data), which Petitioners do not dispute. *See* Pet. 5; Ex.1005 ¶ 32.

The '566 Patent has three independent claims.¹ Independent claim 1 of the '566 Patent recites:

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 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

¹ For purposes of the POPR, 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 '566 Patent claims.

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 at a dose of 2 mg/kg, administered over 30±10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter, 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.

Ex.1004 131:34-67 (claim 1).

Independent claim 3 of the '566 Patent recites:

- 3. 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 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 at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter, 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) $= -2.4 \pm 2.1$ 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.

Id. 132:37-133:12 (claim 3).²

Independent claim 5 of the '566 Patent recites:

5. A method for treating a TNF related condition, wherein the TNF related condition is active ankylosing spondylitis, the method comprising: administering a safe and effective amount of at least one isolated mammalian anti-TNF 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 The use of "Qualify" in the claim language is a clerical error. This limitation refers to ASQoL.

- 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 antibody is administered via intravenous (IV) infusion at a dose of 2 mg/kg, administered 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 Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment.

Id. 133:17-134:20 (claim 5).

The Examiner allowed the claims over the same or similar prior art as advanced by Petitioners, including Inman and van der Heijde. Ex.2002, -017, -022. The Examiner made several anticipation and obviousness rejections, and finally rejected the pending claims as obvious via Wong (Ex.1024) in view of Zhuang (Ex.1038). Ex.2002, -310-12. After fully considering the issues, however, the Examiner found the claims patentable over this prior art. Ex.2002, -383-84.

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. 30. 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. AS and PsA 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 ¶¶ 36-52; *see also supra* Section II.B. These differences lead to different treatment strategies. Ex.2096, 1 (Schett 2011) (“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 also would have collaborated with a team experienced “in pharmaceutical development, such as pharmacokineticists and formulators,” a qualification on which the parties agree. Pet. 30; 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. As explained below, those arguments lack merit because each disputed claim term substantively limits claim scope.³

A. “Treating ... Active Ankylosing Spondylitis” 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

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).

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," the '566 Patent claims recite a method "for treating a TNF related condition, wherein the TNF related condition is active ankylosing spondylitis." 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 ¶ 92.

Later claim limitations, which refer back to the method for treating AS, confirm the preamble's significance. For example, claim 1 later refers to "a patient *treated*," "at 4 weeks of *treatment*," and "at 2 weeks of *treatment*." Ex.1004, 131:63-67 (emphases added). The preamble is limiting because "treating ... active ankylosing spondylitis" 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.").

Finally, the written description consistently emphasizes that treatment of active ankylosing spondylitis is fundamental to the invention. *See, e.g.*, Ex.1004, Title ("Methods for the Treatment of Active Ankylosing Spondylitis"), Abstract ("for use in the safe and effective treatment of active Ankylosing Spondylitis (AS)"), 1:17-21 (Field of the Invention) ("methods utilizing [golimumab] for use in the safe and effective treatment of active Ankylosing Spondylitis (AS)"), 2:61-65 (Summary of the Invention) ("The present invention provides [golimumab] for use in the safe and effective treatment of active Ankylosing Spondylitis."). 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 ankylosing spondylitis is necessary to give meaning to these limitations. *See Eli Lilly*, 8 F.4th at 1342-43.

B. 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. For example, the Examiner initially rejected the pending claims as anticipated by J&J 2016 (Ex.1039) or Janssen 2016 (Ex.1040), noting that the 2016 publication disclosed the claimed clinical endpoints as recited in claims 1, 3, and 5. Ex.2002, -307-08.

This suggests that the Examiner 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. 38)—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.1004, 131:37), selecting appropriate co-administered medications in a “comprising” claim (*see id.* 3:19-21), selecting the “pharmaceutically acceptable carrier or diluent” (*see id.* 131:59-60), selecting the relevant patient population (*see id.* 89:12-94:32), and applying appropriate inclusion and exclusion criteria to obtain the claimed “mean change from baseline” and proportion of patients meeting clinical endpoints (*see id.* 132:67-133:12). Haroon ¶ 94. 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 Petitioner’s 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 ASAS20 at week 16 of treatment.” Ex.1004, 134:21-24. 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 NCT873-V24 Is Prior Art

NCT873-V24 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 February 7, 2017 priority date.

To establish public accessibility, Petitioners assert that NCT873-V24 “was publicly available on ClinicalTrials.gov on October 27, 2015,” citing only the document itself and nearly duplicative statements by their expert to support that alleged posting date. Pet. 23; Ex.1005 ¶ 169. These conclusory assertions are insufficient to establish a reasonable likelihood that it is prior art.

Exhibit 1014 (NCT873-V24) bears the date October 30, 2025 on its first page, far too late to qualify as prior art. Ex.1014, 1. The exhibit is a present-day capture of the clinical trial summary (NCT02186873) and does not show what information was available in 2015. Petitioners offer no corroborating evidence—such as a Wayback Machine capture or server logs—establishing that the portions of Exhibit 1014 purportedly corresponding to “version 24” were available in that form by October 27, 2015.

To the contrary, the Internet Archive's Wayback Machine indicates that it did not capture version 24 until after February 7, 2017. Ex.2064 (Wayback Machine

Calendar of NCT873); *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 NCT873-V24 was "*meaningfully* indexed such that an interested artisan exercising reasonable diligence would have found it." *See Samsung*, 929 F.3d at 1369 (emphasis in original).

In an attempt to fill this gap, Petitioners' expert Dr. Fleischmann asserts that "a POSA searching for studies on 'golimumab' and 'ankylosing spondylitis' would have readily found, among other studies, NCT02186873." Ex.1005 ¶ 169. But Exhibit 1014 itself confirms that NCT02186873 has 35 versions, many of which are dated well after the priority date. Ex.1014, 2-4. Dr. Fleischmann does not verify which versions a POSA purportedly would have found before the priority date, much less establish that version 24 was among them. *See* 37 C.F.R. § 42.65(a); *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 at 15 (PTAB 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. Ex.1005 ¶ 169. But the search functionality available at the relevant time was far more limited. *Compare* Ex.2065 (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 NCT873-V24 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. 26-27; 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.* at 12; *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.” 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). Inherency “may not be established by probabilities or possibilities.” *Rapoport v. Dement*, 254 F.3d 1053, 1063 (Fed. Cir. 2001).

A. NCT873-V24 Does Not Disclose “At Least One Pharmaceutically Acceptable Carrier or Diluent”

Independent claims 1 and 3 require “at least one pharmaceutically acceptable carrier or diluent.” Ex.1004, 131:59-60 (claim 1), 132:63-64 (claim 3). Petitioners concede that “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 3.” Pet. 41. 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. 41-42 (“a POSA also would have known 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. 42. Petitioners thus rely on PI2013-Aria to supply a limitation missing from NCT873-V24. 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. NCT873-V24 Does Not Disclose Administration “Over 30±10 Minutes”

Independent claims 1, 3, and 5 of the '566 Patent require that the anti-TNF antibody is “administered over 30±10 minutes.” Ex.1004, 131:61-62 (claim 1), 132:65-66 (claim 3), 134:16 (claim 5). Petitioners concede “NCT873-V24 does not expressly state that the golimumab was administered over 30±10 minutes,” again improperly relying on the knowledge of a POSA and an additional different reference, PI2013-Aria, to supplant what NCT873-V24 cannot show. Pet. 42. For the same reasons stated above, Petitioners cannot rely on additional references to expand upon NCT873-V24 under a theory of anticipation. *See supra* Section VIII.A.

C. NCT873-V24 Does Not Disclose the Claimed Clinical Endpoints

The independent claims of the '566 Patent require that treatment with golimumab achieve specified clinical endpoints:

- Claim 1: “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” (Ex.1004, 131:63-67);
- Claim 3: “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) $= -2.4 \pm 2.1$ Standard Deviation (SD), Bath Ankylosing Spondylitis Metrology Index (BASMI) $= -0.4 \pm 0.6$ SD, 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS) $= 8.5 \pm 7.5$ SD, 36-item Short-Form Health Survey Mental Component Summary (SF-36 MCS) $= 6.5 \pm 9.1$ SD, and Ankylosing Spondylitis Qualify of Life questionnaire (ASQoL) $= -5.4 \pm 5.0$ SD” (*id.* 132:67-133:12);
- Claim 5: “ $\geq 65\%$ of patients receiving the treatment achieve Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment” (*id.* 134:18-20).

NCT873-V24 discloses none of these claim limitations.

Petitioners attempt to overcome that deficiency through inherent anticipation. They rely on their expert's assertion that, because NCT873-V24 describes the same underlying clinical trial whose endpoints are reported in Example 9 of the '566

Patent, NCT873-V24 “should give the same results.” Ex.1005 ¶ 658. 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 NCT873-V24’s online summary—as briefly described across five pages excluding version numbers and study location—“should give” the same results. Ex.1005 ¶ 658. But the data shows that achieving the claimed clinical endpoints is far from inevitable. For example, claim 1 requires that “a patient” achieves an ASDAS score of < 1.3 at 2 or 4 weeks of treatment. Ex.1004, 131:63-67. Yet to the extent Example 9 discloses the expected results of NCT873-V24, as Petitioners assume, the data show that only some (but not all) patients will achieve an ASDAS score of < 1.3 . *Id.* 107:1-35 (Table 9); *see also* Haroon ¶ 104. 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). Here too, data in the ’566 Patent shows that a patient will not necessarily achieve ASDAS < 1.3 when administered 2 mg/kg golimumab as stated in NCT873-V24. Ex.1004, 107:1-35 (Table 9); *see also* Haroon ¶ 104. A similar analysis applies to the other clinical endpoints of independent claims 3 and 5. *Id.* ¶ 100.

Further, NCT873-V24 would not necessarily achieve the same claimed clinical endpoints because it does not disclose the same patient population in which the ’566 Patent achieved those endpoints. Haroon ¶¶ 70-81, 104-06. The omission of those patient-selection criteria could affect treatment outcomes and yield materially different endpoints from those reported in the ’566 Patent. *Id.*

The claims of the ’566 Patent require treating “active ankylosing spondylitis.” Ex.1004, 131:35 (claim 1), 132:38 (claim 3), 133:18 (claim 5). The specification defines both components of that term—“ankylosing spondylitis” and “active” disease. “Active disease” is evidenced by BASDAI ≥ 4 and VAS ≥ 4 . *Id.* 79:62-65. Example 9 applies those same requirements through key inclusion criteria, including Criterion 5, which requires symptoms of active disease as evidenced by BASDAI ≥ 4 and VAS ≥ 4 . *Id.* 88:47-55, 89:51-54.

NCT873-V24 does not disclose these inclusion criteria. Haroon ¶ 72. Instead, at the time of the invention, a POSA could have applied different definitions of “active disease.” *Id.* ¶ 73. For example, other clinical trials at the time employed different BASDAI level inclusion criteria or omitted BASDAI altogether as an inclusion criterion. *Id.*; *see, e.g.*, Ex.2078 (Haibel 2005). 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 ¶ 74; Ex.2119 (Lord 2009), 566 (Table 3).

NCT873-V24 also does not disclose that the relevant patient population may include up to 10% of patients with “complete ankylosis of the spine” (i.e., complete spinal fusion). Ex.1004, 80:11-16. Dr. Haroon explains that the definition of and threshold for spinal fusion varies across studies. Haroon ¶ 75; *see* Exs.2062-63. Subjects with complete spinal fusion are particularly difficult to treat because their irreversible, advanced disease state limits the likelihood of improvement to clinical endpoints, including ASAS20, BASFI, and BASMI. Haroon ¶ 76.

Nor does NCT873-V24 disclose that up to 20% of subjects may have prior exposure to “one biologic anti-TNF α agent.” *See* Ex.1004, 80:7-10. Other studies commonly required TNF-naïve subjects or different proportions of prior non-responders. Haroon ¶ 76; *see* Exs.2062-63. Prior use and response to such anti-TNF

agents can have a significant impact on clinical efficacy outcomes. Haroon ¶ 78; *see* Ex.2100 (Sieper 2017); Ex.2105 (Abstract) (Taxonera 2017).

NCT873-V24 also does not disclose that efficacy is based on an intent-to-treat analysis, which includes all randomized subjects regardless of protocol adherence. *See* Ex.1004, 82:25-30, 103:18-23. At the priority date, other analytical approaches were common, including per-protocol analysis that considered only subjects who adhered to the protocol. Haroon ¶ 79; *see* Ex.2081, 1021 (Kavanaugh 2014). These differing methodologies can produce different clinical efficacy outcomes. Haroon ¶ 79; Ex.2071 (Bai 2021) (Abstract).

Finally, NCT873-V24 states that additional inclusion and exclusion criteria apply, yet does not identify them. Ex.1014, 8-9 (“Additional protocol-defined inclusion criteria apply” and “[a]dditional protocol-defined exclusion criteria apply.”). As Dr. Haroon explains, such criteria could include requirements relating to MRI-based eligibility or prior primary failure of anti-TNF therapy, each of which can materially affect clinical efficacy outcomes. Haroon ¶ 81. Because NCT873-V24 omits parameters that can significantly affect its achievement of the 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. *Apotex*, IPR2022-01524, Paper 9 at 36-37. In that case (as here, *see* Haroon ¶¶ 70-81, 104-06), 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 NCT873-V24 and PI2013-Aria (Ground 2)

In Ground 2, Petitioners seek to combine NCT873-V24 with the label for IV administration of golimumab to treat RA (PI2013-Aria). That combination fares no better than NCT873-V24 alone.⁴

Petitioners concede that “neither NCT873-V24 nor PI2013-Aria disclose the claimed clinical outcomes.” Pet. 48. And, as discussed above, NCT873-V24 does

⁴ As a threshold matter, Petitioners failed to show these references were prior art.

See supra Section VII.

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 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* Ex.2033, 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 NCT873-V24 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.

X. Petitioners Fail to Establish a Reasonable Likelihood of Prevailing on Obviousness Arguments Over NCT873-V24, PI2013-Aria, PI2015-Simponi, Van der Heijde, and Inman (Ground 3)

It is telling that Petitioners must rely on five 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 if taken together, the five prior art references (NCT873-V24, PI2013-Aria, PI2015-Simponi, van der Heijde, and Inman) do not disclose all claim limitations, (2) there would have been no motivation to combine the five references in the manner proposed, and (3) there was no reasonable expectation of success.

A. NCT873-V24, PI2013-Aria, PI2015-Simponi, Van der Heijde, and Inman Do Not Disclose the Claimed Clinical Endpoints

Petitioners admit that NCT873-V24 and PI2013-Aria do not disclose the claimed clinical endpoints. Pet. 48 (“neither NCT873-V24 nor PI2013-Aria disclose the claimed clinical outcomes”). The remaining three references, all of which

concern SC administration of golimumab, likewise fail to disclose the claimed clinical endpoints.

Independent claim 1 requires achieving ASDAS < 1.3 after only 2 or 4 weeks of treatment. Ex.1004, 131:62-67. Petitioners rely on van der Heijde for its disclosure of ASDAS inactive disease (< 1.3) at weeks 14 and 24. Pet. 51. That disclosure falls well short of the claimed clinical endpoint. Unlike the '566 Patent, which provides a rapid clinical effect and achieves the claimed clinical endpoint within 2 or 4 weeks, van der Heijde reports inactive disease only after prolonged administration of golimumab (through a different route of administration) over many additional weeks and months. Haroon ¶¶ 109-14.

Nor would a POSA have reasonably expected the claimed IV administration of golimumab to achieve such dramatically faster results, particularly in light of contemporaneous studies reporting lower efficacy with IV administration than with SC administration. Rutgeerts 2015, 504; *see also* Haroon ¶ 114; *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 (among other endpoints) achieving SF-36 PCS= 8.5 ± 7.5 at week 16 of treatment. Ex.1004, 132:67-133:12. Petitioners

again rely on van der Heijde, this time for its disclosure of SF-36 PCS scores of 8.8 ± 9.6 and 8.9 ± 9.8 at week 14. Pet. 56. In addition to the different route of administration, van der Heijde fails to report the SF-36 PCS endpoint at the claimed week 16 timepoint. 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.

Furthermore, the clinical endpoint data reported in van der Heijde and Inman is based on a different and easier-to-treat patient population. Haroon ¶ 116. Unlike the '566 Patent, van der Heijde and Inman excluded subjects with complete ankylosing spondylitis and subjects with any prior exposure to anti-TNF therapy. *Id.* By excluding those more difficult-to-treat patients, van der Heijde reported SF-36 PCS values that are artificially elevated and not comparable to the values recited in claim 3. *Id.* For that reason as well, van der Heijde does not disclose the claimed clinical endpoint of claim 3. *Id.*

Independent claim 5 requires that $\geq 65\%$ of patients achieve ASAS20 at week 16 of treatment. Ex.1004, 134:18-20. Petitioners rely on Inman for its disclosure that 59.4% and 60% of patients achieved ASAS20 at week 14. Pet. 58. Neither value meets the claimed threshold of $\geq 65\%$, and thus the claim limitation is not disclosed. Haroon ¶¶ 119-24.

Petitioners attempt to dismiss these deficiencies as “small differences.” Pet. 59. 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' five-reference combination is to combine NCT873-V24 (directed to treatment of AS) 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 AS 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 NCT873-V24 can be combined with PI2013-Aria because both are “used for the same purpose—to treat a TNF- α related disease in humans.” Pet. 47. This broad generalization fails because TNF plays materially different roles in each disease. Haroon ¶¶ 36-43; *see also supra* Section II.B.

Petitioners’ argument that the references should be combined because they “are both Janssen publications” (Pet. 47) 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 NCT873-V24 and PI2013-Aria, Petitioners next try to add PI2015-Simponi, van der Heijde, and Inman to the combination, claiming they would be combined because they “relate to using golimumab for the treatment of AS.” Pet. 54. But those three references disclose only SC administration of golimumab, not the claimed IV administration. Haroon ¶¶ 129-30. 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. 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

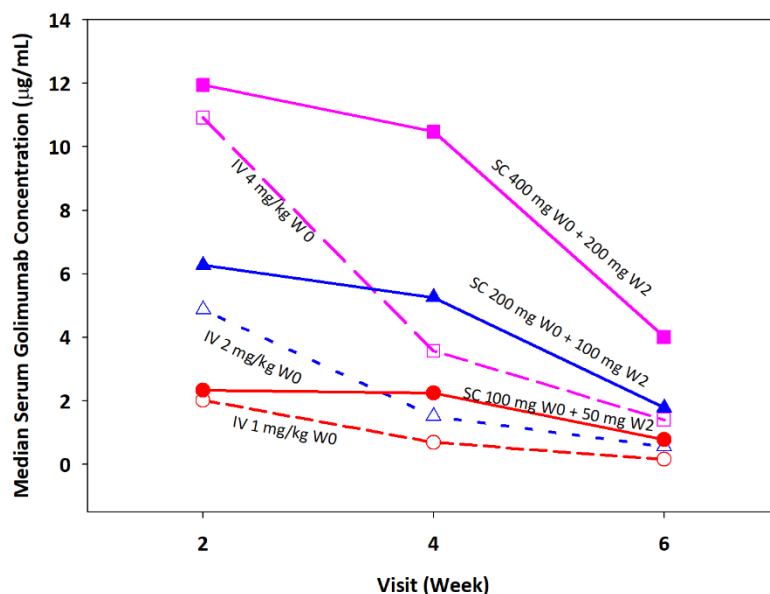
Petitioners rely on studies of SC golimumab (PI2015-Simponi, Inman, van der Heijde) and IV golimumab for a different disease (PI2013-Aria), together with nothing more than a protocol proposing to study IV golimumab in AS (NCT873-V24). Such evidence cannot support a reasonable expectation of success.

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. 58 (Inman discloses “a lower number than the claimed percentage of patients achieving ASAS20 with IV golimumab at week 16”). Instead, Petitioners argue that the claimed clinical endpoints would have been obvious because “IV

golimumab has a higher bioavailability, $C_{\max}$, and AUC than SC golimumab.” Pet. 53, 56.

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.2094), the investigators measured serum golimumab concentrations for IV and SC dosage regimens that “were expected to provide comparable systemic drug exposure.” *Id.* 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.2095):

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 ¶¶ 59-61. 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 Inman, van der Heijde, 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, 3406 (Figs. 2-3) (Inman); Ex.1033, 1099 (Fig. 1) (van der Heijde);

Ex.1042, 2513 (Fig. 3) (Kavanaugh 2012). PI2015-Simponi likewise states that there was “no clear evidence of improved ASAS response with the higher SIMPONI dose group (100 mg) compared to the lower SIMPONI dose group (50 mg).” Ex.1015, 29. 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 ¶¶ 59-62, 131-33. 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 (“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 ¶ 133. 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. 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.

XI. Conclusion

For the reasons set forth above, Janssen respectfully requests that the Director 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 11,631 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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