

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME LLC,

Petitioner,

v.

SURROZEN OPERATING, INC.,

Patent Owner.

Case No. PGR2026-00027

Patent No. 12,297,278

**PETITIONER'S OPPOSITION
TO PATENT OWNER'S DISCRETIONARY-DENIAL REQUEST**

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GLOSSARY

<i>Bold and italicized</i>	Emphasis added unless otherwise indicated
Patent or '278 patent	U.S. Patent No. 12,297,278
Patent Owner	Surrozen Operating, Inc.
Petitioner	Merck Sharp & Dohme LLC
POSA	Person of ordinary skill in the art
Rule 42.104(b)(4) Enforcement Memo	Memorandum from Director Coke Morgan Stewart, Enforcement and Non-Waiver of 37 C.F.R. § 42.104(b)(4) and Permissible Uses of General Knowledge in Inter Partes Reviews, 1 (July 31, 2025) (uspto.gov/sites/default/files/documents/aapa_memo_final_signed.pdf)

I. Introduction

Petitioner challenged the '278 patent within nine months of issuance. Paper 1 (“Petition” or “Pet.”); Paper 3; EX1001, code (45) (issued May 13, 2025). As the Director has found, such challenges “are favored because they ... are close in time to examination, and occur before expectations in the patent rights are strongly settled.” *Multi-Color Corp. v. Brook & Whittle Ltd.*, PGR2025-00025, Paper 10 at 2-3 (Director July 16, 2025) (precedential). Here, the points raised in Patent Owner’s Request (Paper 8 (“PODD”)) only underscore why institution should be granted: this early filed challenge, brought before any settled expectations could take hold, squarely presents issues the Office did not previously resolve and material errors bearing directly on patentability.

First, there is no co-pending litigation implicating 35 U.S.C. § 314(a) considerations for this favored “*alternative* to district court patent litigation for resolving disputes over patent validity.” *Magnolia Medical Technologies, Inc. v. Kurin, Inc.*, IPR2026-00097, Paper 17 at 2 (Director May 14, 2026) (precedential) (“The purpose of AIA reviews was, and is, to provide a quick and cost-effective *alternative* to district court patent litigation for resolving disputes over patent validity.”). Beyond implicitly recognizing validity issues to be resolved, Patent Owner’s argument that a jury is better positioned than the Board to hear the dispute thus has no merit. *See* PODD, 2; *infra* Section II, V.

Second, Patent Owner does not show that *any* of Petitioner’s 35 U.S.C. § 112 arguments in Ground 1 (all claims lack written description), Ground 2 (all claims lack enablement), or Ground 3 (all claims are indefinite) were “previously ... presented to the Office.” *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential) (“*Advanced Bionics*”). Patent Owner cannot, as it has, merely “assume [that] the Examiner ... considered the specific written description[,] [enablement, and indefiniteness] issue[s] presented here, and further decided [those] issue[s] in favor of Patent Owner” where “such consideration and decision are not expressly set forth in the prosecution history record.” *Schul Int’l Co., LLC v. Emseal Joint Sys., Ltd.*, PGR2018-00034, Paper 7 at 19 (PTAB Aug. 22, 2018) (instituting PGR); *infra* Section III.

Third, while certain obviousness arguments relying on the Garcia reference (EX1004) of Ground 4 (anticipation of claims 1, 4) were addressed during prosecution, the Examiner overlooked Garcia’s anticipatory disclosure of “dimer[s]” of its bivalent Wnt surrogate molecules. EX1008, 4170-71. That the Examiner erred in finding that Garcia “does not teach dual variable domain (DVD) format of bispecific antibody” (PODD, 8-9) is confirmed by a named inventor’s representations that bivalent molecules formed as “described by Garcia” “aggregat[e]” (dimerize) to tetravalent species with “two ... binding domains for

FZD and two ... binding domains for LRP in one molecule” that were “associated with Wnt activity”(EX1008, 4170-71), as claimed. “Discretionary denial is not appropriate” here where “the patent examiner overlooked” Garcia’s anticipatory dimer disclosure. *Eunsung Global Corp. v. Hydrafacial LLC*, IPR2025-00445, Paper 14 at 3 (Director July 10, 2025); *infra* Section IV.

Finally, Patent Owner’s “extensive reliance on expert testimony” argument (PODD, 19-20) provides no basis for discretionary denial. Critically, “Patent Owner does not identify any portions of the expert testimony that suggest Petitioner is using its expert to fill gaps in the prior art.” *Cambridge Indus. USA, Inc. v. Applied Optoelectronics, Inc.*, IPR2025-00437, Paper 10 at 2 (Director June 26, 2025) (denying discretionary denial); *infra* Section V.

At bottom, discretionary denial is not warranted for this early challenge to address issues not previously presented to the Office and resolve material errors attendant to the patent’s allowance.

II. Petitioner’s Early Challenge Favors Referral as Patent Owner Has Not Developed Settled Expectations

Petitioner’s early challenge—within nine months of issuance—is “favored” because it is “close in time to examination, and occur[red] before expectations in the patent rights are strongly settled.” *Multi-Color Corp.*, PGR2025-00025 at 2-3; Pet. 92-94; EX1001, code (45) (issued May 13, 2025). Indeed, Patent Owner does not claim any settled expectations or present arguments against an early challenge.

This PGR was also filed in the absence of parallel litigation. Pet., 92; Paper 4 at 3. This further favors referral and institution as “there is no concern of inconsistent outcomes or significant duplication of efforts resulting from two proceedings operating in parallel.” *Intas Pharms. Ltd. v. Atossa Therapeutics, Inc.*, IPR2025-00799, Paper 12 at 2-3 (PTAB Aug. 12, 2025) (denying request for discretionary denial where “the parties are not involved in a parallel proceeding involving the challenged patents”); *Azurity Pharms., Inc. v. Helsinn Healthcare S.A.*, IPR2025-00945, Paper 11 at 2-3 (Director Sept. 19, 2025) (absence of “parallel proceeding involving the challenged patents” weighs against discretionary denial).

In the absence of settled expectations or parallel litigation, the Petition’s early challenge thus weighs heavily in favor of referral.

III. Grounds 1-3 under 35 U.S.C. § 112 Were Not Previously Presented and Are Necessitated by the Examiner’s Material Error

A. Petitioner’s Arguments Were Not Previously Presented

Petitioner’s § 112 arguments in Ground 1 (no full scope written description), Ground 2 (full scope not enabled), and Ground 3 (indefiniteness) were not previously presented to or addressed by the Office. Pet., 24-87. Discretionary denial is therefore unwarranted as *Advanced Bionics* Step 1 is not met.

Without any evidence from the prosecution record, Patent Owner argues that “the Examiners evaluated the patent claims for conformance with § 112” and

“understood the claims were sufficiently supported.” *See* PODD, 13–16. Patent Owner is wrong, however, to “assume [that] the Examiner correspondingly considered the specific [§ 112] issue[s] presented here, and further decided [those] issue[s] in favor of Patent Owner” where “such consideration and decision are not expressly set forth in the prosecution history record.” *Schul Int’l Co., LLC*, PGR2018-00034 at 19 (“Invoking 35 U.S.C. § 325(d) as a categorical matter to deny review on the basis of such an assumption would render 35 U.S.C. § 321(a) a nullity regarding post-grant review of compliance with the written description requirement.”) (instituting PGR). Even if *some* § 112 issues had been considered, institution would still be warranted as Patent Owner does not—and cannot—assert that the specific invalidity basis in Petitioner’s Ground 1-3 were addressed. *Merck Sharp & Dohme LLC v. Halozyme, Inc.*, No. PGR2025-00003, Paper 25 at 21 (PTAB June 2, 2025) (rejecting patent owner’s § 325(d) argument where the examiner had rejected the claims under § 112 but did not address the specific “breadth of the claimed modified PH20 polypeptide” issue raised in the petition); *Beigene USA, Inc. v. Pharmacyclics LLC*, No. PGR2024-00009, Paper 9 at 40-41 (PTAB May 1, 2024) (instituting PGR and finding that “Patent Owner has not satisfied the first prong of *Advanced Bionics*” where the examiner had considered other § 112 issues but where “it appears ... that the Examiner may not have considered” the specific issues raised in the petition).

B. Allowance Reflects Examiner's Material Error

Because the Petition's § 112 arguments were not previously presented during prosecution, it is unnecessary to proceed to *Advanced Bionics* Step 2. *Advanced Bionics*, at 8. Nevertheless, discretionary denial is also unwarranted under Step 2 in view of material error with respect to each of Grounds 1-3.

1. "Wnt surrogate molecule" Is Expressly Defined in the Specification and Was Relied upon to Distinguish Prior Art

Patent Owner argues that the Petition's § 112 grounds rest on a "tenuous" construction that the "Wnt surrogate molecule" preamble is (1) limiting and (2) expressly defined in the specification. PODD, 17. In support, Patent Owner invokes "plain and ordinary" meaning arguments irrelevant given the patent's express lexicography, an imagined "high burden" to construe the preamble as limiting, and inapplicable "intended use" generalizations. PODD, 17-18 (citations and quotations omitted). Yet Patent Owner ignores the intrinsic evidence demonstrating that the "Wnt surrogate molecule" preamble is expressly defined in binding lexicography and was relied upon as limiting. Petition, 17-19.

To start, Patent Owner does not dispute that the Petition's construction of "Wnt surrogate molecule" is verbatim based on the patent's express lexicography:

Wnt surrogate molecules of the present invention are biologically active in binding to one or more Fzd receptor and to one or more of LRP5 and LRP6, and in activation of Wnt signaling, i.e., the Wnt surrogate molecule is a Wnt agonist. The term "Wnt agonist activity" refers to the ability

EX1001, 16:52-56 (highlighting added); Pet. 17. This definition “of the present invention” is textbook lexicography. *Trading Techs., Int’l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1353-54 (Fed. Cir. 2010); *Honeywell Int’l, Inc. v. ITT Indus., Inc.*, 452 F.3d 1312, 1318 (Fed. Cir. 2006).

Patent Owner also does not dispute that the preamble’s functional property of being a Wnt agonist was relied on during prosecution as “an important biological distinction” to overcome a prior art rejection. EX1008, 4006; Pet. 18. That the “Wnt surrogate molecule” preamble is not merely an intended use was reinforced by named inventor Dr. Li, who represented during prosecution that “the claimed molecules ... agonize” Wnt signaling. EX1008, 4168 (emphasis in original); EX1002, ¶106; EX1003, ¶¶73-74; Pet. 18. This collective evidence “transforms the preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention.” *Catalina Mktg. Int’l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002); Pet. 18.

2. Examiner’s Written Description, Enablement, and Definiteness Material Errors

The functionally defined “Wnt surrogate molecule” preamble applies to the extremely broad genus of tetravalent, multispecific molecules lacking meaningful structural features or limitations, such as any required amino acid sequences. The claimed Fzd and Lrp binding regions are defined solely by function. EX1002, ¶¶102-05, 141-42, 211; EX1003, ¶¶5, 67-69, 71. Their topology (spatial

arrangement) and format (types of antibody derived segments and linkers) are unlimited, except that “each of the two LRP5/6 binding regions is fused to one of the two Fzd binding regions via a linker moiety” that itself is unlimited in structure, composition, sequence, rigidity, or length. EX1002, ¶¶108, 120-22, 212-13; EX1003, ¶¶117-18. Separately and in combination, the biological activity required by the preamble and the massive functionally defined genus lead to three § 112 defects, each of which reflects material error by the Examiner. *See e.g., Inari Agriculture, Inc. v. Corteva Agriscience LLC*, No. PGR2023-00022, Paper 11 at 15-16 (PTAB Oct. 13, 2023) (instituting where the examiner materially erred “in not issuing a rejection for enablement”).

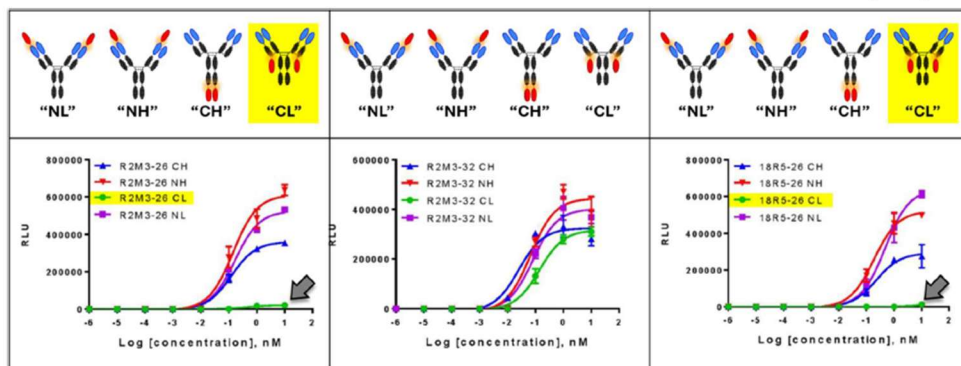
For context, the field of Wnt biology was nascent and unpredictable as of the ’278 patents filing date (Dec. 2017). Pet. 4-6. “[A] number of factors [had] thwarted progress in this field,” including that “the WNT signalling cascade is bewilderingly complex.” EX1043, 1; EX1063, 1; EX1003, ¶¶2, 76-100; EX1002, ¶¶74-75. This is confirmed in Patent Owner’s new EX2003, which explains that “the complexity and redundancy of the Wnt signaling pathways pose significant challenges for research and targeted therapies.” EX2003, 31. And, in contrast to the unlimited scope of the ’278 patent claims with respect to specific tissues or cell types, EX2003 explains that “[t]he role of Wnt signaling varies across different tissues and cell types, necessitating tailored therapeutic strategies” and that “Wnt

signaling can either promote or inhibit [disease] progression, depending on the context.” EX2003, 17, 31. Notably, while EX2003 addresses some Wnt antagonists, it does not identify *any* surrogate Wnt *agonists* as required for the claimed “Wnt surrogate molecules.” *E.g.* EX2003, 26-29 (Tables 4-5, describing only putative antagonists).

Grounds 1 and 2 are necessitated by the Examiner’s material errors in overlooking the absence of sufficient written description and enablement, respectfully, for the extraordinarily broad, functionally defined genus where the specification lacks a representative number of species or a common structural feature across all its encompassed formats. *Merck Sharp & Dohme LLC*, PGR2025-00003 at 21; *Inari Agriculture, Inc.*, PGR2023-00022 at 15-16. Patent Owner provides no basis to dispute the Examiner’s error in overlooking that the specification explores only a small, non-representative subset of formats, targets, and linkers, and leaves the effects of key features such as geometry, stoichiometry, linker design, and epitope choice to undue trial-and-error experimentation making and screening massive numbers of candidates across multiple assays, cell types, and conditions. Pet. 24–62; EX1002, ¶¶214-16, 221-31; EX1003, ¶¶124-143.

For example, the specification shows that assay responses unpredictably depend on the specific binding region sequences and the specific formats in which they are combined. EX1002, ¶¶189-90; EX1003, ¶122. This is evident in the

figure below, where each panel compares molecules with the same Fzd and Lrp binding sequences (e.g., “R2M3” and “26,” respectively) arranged in four different tetravalent formats (“NL,” “NH,” “CH,” and “CL”).

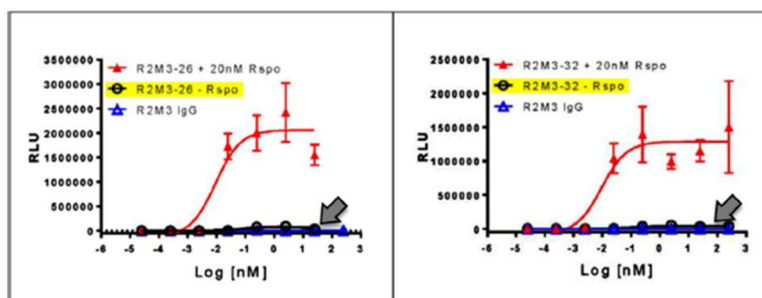


EX1001, Figures 9A (R2M3, 26), 9B (R2M3, 32), 9C (18R5, 26) (annoated). The “CL” format was only shown assay-active with a specific pair of Fzd and Lrp5/6 binding sequences: R2M3 and 32, respectively (middle panel). Other binding pairs showed no activity in the “CL” format, notwithstanding assay activity in “NL,” “NH,” and “CH” formats (R2M3 and 26 (left panel); 18R5 and 26 (right panel)). The ’278 patent admits that “[t]hese results demonstrate that the attachment location of the fusion and the geometry between the Fzd and LRP binding domains play roles in the ability of Wnt surrogates to activate Wnt signaling.” EX1001, 157:44-50. The ’278 patent, however, fails to provide guidance beyond trial-and-error experimentation to account for these interdependent effects on “the ability ... to activate Wnt signaling.” *Id.*; EX1002, ¶169; Pet. 62–75. Irreconcilable with the unpredictable variability in the ability to activate Wnt signaling and absence of

guidance in the specification, the claims are not limited to particular Fzd and LRP binding domain attachment locations or geometry—leading to a failure of both the written description and enablement requirements. EX1002, ¶¶195-96, 215.

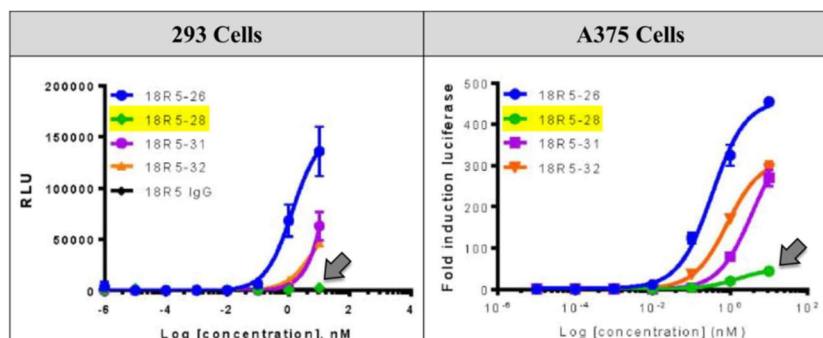
Ground 3 is similarly necessitated by the Examiner’s material error in failing to address the indefiniteness of all claims, including the lack of reasonable certainty as to the scope of “biologically active ... in activation of Wnt signaling” and acting as a “Wnt agonist.” EX1002, ¶¶2, 10, 236-46; EX1003, ¶¶4, 9-10, 144-55. Rather than providing basis to dispute the Examiner’s error in this regard, Patent Owner highlights the indefiniteness when asserting that specification’s tetravalent molecules all “successfully agonized the Wnt pathway.” PODD, 19.

As an initial matter, Patent Owner is incorrect. For instance, several of the candidate molecules failed to activate Wnt signaling in the absence of R-spondin, indicating that, unlike natural Wnt and non-Wnt ligands, they are not “biologically active.” EX1003, ¶149. This is evident in the ’278 patent’s figures below showing no appreciable difference without R-spondin (“- Rspo”) between claimed tetravalent “R2M3-26” and “R2M3-32” molecules and unclaimed R2M3 IgG (lacking Lrp binding regions) that according to the specification “did not induce reporter activity.” EX1001, 155:35-36, 155:65.



EX1001, Figures 2D, 3D (annotated). Patent Owner’s inconsistent assertion that R2M3-26 and R2M3-32 “successfully agonized the Wnt pathway” (PODD, 19) thus reinforces the absence of reasonable certainty in the meaning of “Wnt surrogate.” Pet. 60-61; EX1002, ¶¶186-96; EX1003, ¶¶144-54; *see also* Pet. Figs. 7, 10-12, 14-16 (highlighting additional tetravalent formats that failed to activate Wnt signaling).

Patent Owner’s assertion also fails to address the core indefiniteness deficiency in that the specification provides no metric for “successfully agonized” and instead reports conflicting assays results that depend on myriad undefined conditions, including the cell type assayed and the presence or absence of R-spondin. Pet. 48, 70-71, 81-82; EX1002, ¶¶206-08, 236, 242-43; EX1003, ¶¶147-51. In one set of assays, for example, the specification’s “18R5-28” candidate molecule showed only a flat line response (no apparent Wnt signaling activity) compared to other molecules in “293 Cells” (left panel below) but showed a visible response in “A375 Cells” (right panel below). EX1002, ¶243; EX1003, ¶151.



EX1001, Figures 6A and 6B (annotated). Because of inconsistencies like these and the absence of guidance as to determinative assay conditions or response levels, a skilled artisan would not understand with reasonable certainty whether a given candidate molecule qualifies as a Wnt surrogate molecule. EX1002, ¶243; EX1003, ¶¶150-51; *Akamai Techs., Inc. v. MediaPointe, Inc.*, 159 F.4th 1370, 1379 (Fed. Cir. 2025) (“We have repeatedly said that when multiple methods for determining whether a claim limitation is met lead to different results without guidance as to which method should be used, the claim is indefinite.”) (cleaned up). The Examiner thus erred in failing to find all claims indefinite.

Patent Owner’s reliance on *Teva Pharm. Int’l GmbH v. Eli Lilly & Co* (PODD, 18-19) is inapt as it omits a key finding that “[t]he asserted claims are to methods” of treatment using compounds that “were well known in the prior art and disclosed in the specification.” 172 F.4th 1367, 1376, 1378 (Fed. Cir. 2026) (“*Teva Pharm.*”). Here, by contrast, the claims are directed to functionally defined “Wnt surrogate molecules” themselves—not methods of treatment—and Patent Owner has strenuously asserted that its claimed tetravalent molecules had not even

been “contemplated.” *See, e.g.*, EX1008, 4006-7 (“the need of a tetravalent, multi specific format for Wnt surrogate molecules was neither taught nor contemplated”), 4168 (“[T]he understanding in the art at the time of the present invention actually teaches away from the claimed tetravalent Wnt surrogate molecules, with 2:2 stoichiometry.”).

The *Teva Pharm.* panel decision also does not purport to, and indeed cannot, supersede the Examiner’s material error in view of earlier and binding precedent. *See e.g., Amgen Inc. v. Sanofi*, 598 U.S. 594, 614 (2023) (genus not enabled where the specification leaves a POSA to engage in extensive trial-and-error experimentation to identify which embodiments work); *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1358 (Fed. Cir. 2010) (en banc) (written description not satisfied by disclosure of a desired function without demonstrating possession through representative species or common structural features); *Juno Therapeutics, Inc. v. Kite Pharma Inc.*, 10 F.4th 1330, 1340-42 (Fed. Cir. 2021) (limited number of examples does not support a functionally defined genus where the universe of embodiments is vast and success depends on unpredictable structural features); *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301 (Fed. Cir. 2014) (highly similar species in one corner of a broad functional genus do not provide written description support for claims covering the entire genus in an unpredictable art); *Idenix Pharmaceuticals LLC v. Gilead Sciences Inc.*, 941

F.3d 1149 (Fed. Cir. 2019) (written description insufficient where the specification “provide lists or examples of supposedly effective nucleosides, but do[es] not explain what makes them effective, or why”); *Seagen Inc. v. Daiichi Sankyo Co.*, 160 F.4th 1322, 1329 (Fed. Cir. 2025) (genus claims covering millions of possible embodiments not enabled where the art is unpredictable and the specification provides no general rule distinguishing functional from nonfunctional embodiments); *Baxalta Inc. v. Genentech, Inc.*, 81 F.4th 1362, 1366 (Fed. Cir. 2023) (genus not enabled where a POSA must generate and screen millions of candidate antibodies to determine which satisfy the claimed functional requirements); *cf. Teva Pharm.*, at 1377 (distinguishing claims to “a well-known genus used as part of a different invention”). *Teva Pharm.* further fails to address § 112(b) indefiniteness and is thus irrelevant to the Examiner’s error in Ground 3.

Because Grounds 1–3 present legal and factual questions erroneously overlooked during prosecution, discretionary denial is unwarranted.

IV. Ground 4 Addresses the Examiner’s Material Error in Failing to Recognize or Apply Garcia’s Disclosure of Anticipatory “Dimers”

Patent Owner argues that “[t]he Petition ... raises arguments about Garcia US’s teachings that the Examiners expressly considered” in stating that “Garcia [US] does not teach dual variable domain (DVD) format of bispecific antibody.” PODD, 8-9 (emphasis omitted), *quoting* EX1008 at 2973, 3983. Rather than providing a basis for discretionary denial, the Examiner’s statement reflects the

material error of overlooking Garcia’s disclosure of claimed tetravalent species—dimerized proteins consisting of two Fzd binding regions and two Lrp5/6 binding regions. Pet. 88-91; EX1002, 257-62. “Discretionary denial is not appropriate” because “the patent examiner overlooked” these anticipatory disclosures. *Eunsung Global Corp.*, IPR2025-00445 at 3; *CSPC Pharm. Grp. Ltd. v. Ipsen Biopharm Ltd.*, IPR2025-00505, Paper 11 at 3 (PTAB July 16, 2025) (examiner erred by overlooking disclosure of “critical limitations in the claims” of reference applied during prosecution).

There is no dispute that Garcia discloses bivalent and multispecific Wnt polypeptides “where a binding domain for Fzd is joined to a binding domain for Lrp5/6.” EX1004, [0056]; Pet. 88; PODD, 11-12. There is also no dispute that two of these bivalent polypeptides together—a dimer—would be tetravalent and multispecific as claimed. EX1002, ¶257 (“[A] dimer formed from two such polypeptides contains two binding regions for Fzd and two binding regions for Lrp5/6. Because this dimer contains four antigen-binding regions, it is a tetravalent molecule.”); Pet. 88-91.

While Patent Owner recycles its prosecution argument that Garcia only discloses bivalent 1:1 Fzd:LRP5/6 polypeptides, Garcia is not so limited. PODD, 12; EX1008 at 4005, 4168; Pet. 31, 87, 90. To the contrary, Garcia expressly discloses dimerization of its bivalent polypeptide molecules, i.e., that its

*“polypeptide Wnt surrogate may be a single chain, **dimer**, or higher order multimer.”* EX1004, [0056] (emphasis added); Pet., 88. Dimers of Garcia’s bivalent Fzd:LRP5/6 polypeptides are tetravalent and multispecific, as claimed. EX1002, ¶257-62.

Confirmation that Garcia discloses tetravalent and multispecific Wnt surrogates based on the aggregation (dimerization) of its bivalent “tandem scFv format” polypeptides is found in the Rule 132 declaration of the ’278 patent’s named inventor, Dr. Li. EX1002, ¶¶258-59; EX1008, 4170. In relevant part, Dr. Li represented that he made compositions comprising a “tandem scFv format” with “a single scFv Fzd binding linked to a single scFv Lrp5/6 binding” as “described by Garcia.” EX1008, 4170. Dr. Li further confirmed that the “aggregation of two ... tandem scFv molecules,” corresponding to a tetravalent species with “two ... binding domains for FZD and two ... binding domains for LRP in one molecule,” was “associated with Wnt activity.” *Id.*, 4171. In other words, Dr. Li confirmed that a dimer of two of Garcia’s tandem scFv format was tetravalent—having *two* Fzd binding regions and *two* Lrp5/6 binding regions—and activated the Wnt signaling pathway. EX1002, ¶259.

Patent Owner characterizes Merck’s position as “mere disagreement” with the Examiner. PO Br. 9–10. Not so. As above, Merck’s anticipation ground relies on Garcia’s express disclosure, including that “a polypeptide Wnt surrogate may

be a ... dimer” and confirmation from Patent Owner’s inventor that this corresponds to a tetravalent species with two Fzd binding domains and two Lrp5/6 binding domains associated with Wnt activity. EX1004, [0056]; Pet. 10. The Examiner’s error in having overlooked Garcia’s express disclosure constitutes material error, not “mere disagreement.” *See Eunsung Global Corp.*, IPR2025-00445 at 3 (“[T]he patent examiner overlooked certain teachings in [examiner-considered prior art] that appear to disclose the allowable features of the claims. Discretionary denial is not appropriate for this reason.”).

Patent Owner also insinuates that “Petitioner attempts to bury this ground.” PODD, 7. This misdirected disparagement ignores that Grounds 1-3 are dispositive of all claims (1-5) while Ground 4 is limited to claims 1 and 4.

V. Petitioner’s Experts Are Properly Relied Upon, Without Improper Gap Filling

Patent Owner’s “extensive reliance on expert testimony” argument (PODD, 19-20) lacks any merit as it fails to “identify any portions of the expert testimony that suggest Petitioner is using its expert to fill gaps in the prior art.” *Cambridge Indus. USA, Inc.*, IPR2025-00437 at 2 (denying patent owner’s discretionary denial request). Indeed, Patent Owner does not dispute that Petitioner’s expert testimony is properly used, such as “to demonstrate the knowledge of a person having ordinary skill in the art.” Rule 104(b)(4) Enforcement Memo.

For example, Patent Owner characterizes Petitioner’s expert testimony as “cast[ing] aspersions on the assays disclosed in the specification” but not as improper gap filling in the prior art. PODD, 20. Rather than being gap filling, this testimony address the knowledge and understanding of a POSA regarding condition-dependent assay results and variability, including that:

As explained above, notwithstanding the known assay dependence as of 2017, the specification of the ’278 patent does not specify any particular assay or assay conditions for measuring canonical or noncanonical Wnt signaling. Although the ’278 patent reports results generated using a TOPFlash assay, that assay itself is condition dependent, and the specification does not endorse any specific TOPFlash assay conditions. *See supra* Sections V.A, IX.B, X.B. Rather, the ’278 patent presents conflicting TOPFlash assay data regarding whether a candidate molecule qualifies as a “Wnt surrogate molecule,” with the outcome varying based on assay conditions, including the cell type used, the particular Fzd and Lrp5/6 receptors expressed, the presence or absence of potentiators such as R-spondin, and the concentrations tested.

EX1003, ¶144. Neither this nor any other portions of Petitioner’s expert testimony is—or is even alleged by Patent Owner to be—substantively improper.

Patent Owner’s suggestion that the Board is less capable than a jury for the present dispute (PODD, 2) should also be rejected. *Microsoft Corp. v. IPA Techs., Inc.*, IPR2019-00812, Paper 44 at 170 (PTAB Oct. 15, 2020) (“[T]he Board, sitting

as a non-jury tribunal with particular administrative and technical expertise, is not as vulnerable to being misled or prejudiced as a jury might, and is well-positioned to determine and assign appropriate credibility and weight to the evidence presented at trial”). Indeed, the present early challenge before the Board is a “favored” form of adjudication. *Multi-Color Corp.*, PGR2025-00025 at 2-3.

Patent Owner’s conclusory attorney argument regarding expert testimony and jury superiority thus fails to provide any basis to deny institution.

VI. Conclusion

Especially in the absence of settled expectations, referral and institution of this PGR are warranted to address unresolved statutory deficiencies and errors underlying allowance of the ’278 patent.

Dated: May 26, 2026

By: / Mark J. Feldstein /
Mark J. Feldstein, Lead Counsel
Reg. No. 46,693

CERTIFICATE OF SERVICE

The undersigned certifies that a copy of the foregoing **Petitioner's Opposition to Patent Discretionary-Denial Request** was served on May 26, 2026, via email directed to counsel of record for the Patent Owner at the following:

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