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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANOFI-AVENTIS U.S. LLC, GENZYME CORP., and REGENERON PHARMACEUTICALS, INC.,
Petitioner,

v.

IMMUNEX CORPORATION,
Patent Owner.

Case IPR2017-01879
Patent 8,679,487 B2

Before JAMES T. MOORE, GRACE KARAFFA OBERMANN, and TINA E. HULSE, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Sanofi-Aventis U.S. LLC, Genzyme Corp., and Regeneron Pharmaceuticals, Inc. (collectively, "Petitioner") filed a Petition requesting an *inter partes* review of claims 1–14, 16, and 17 of U.S. Patent No. 8,679,487 B2 (Ex. 1001, "the '487 patent"). Paper 1 ("Pet."). Immunex Corporation ("Patent Owner") filed a Preliminary Response to the Petition. Paper 10 ("Prelim. Resp."). With our authorization, Petitioner filed a Reply to the Preliminary Response (Paper 13, "Reply"), and Patent Owner filed a Surreply (Paper 15, "Surreply").

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon considering the Petition and Preliminary Response, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–14, 16, and 17 of the '487 patent. Accordingly, we institute an *inter partes* review of those claims.

A. Related Proceedings

Patent Owner has asserted the '487 patent against Petitioner in a pending lawsuit styled *Immunex Corp. v. Sanofi*, No. 2:17-cv-02613 (C.D. Cal., filed April 5, 2017). Pet. 9; Paper 7, 2.

Petitioner has also filed a petition for *inter partes* review of the '487 patent on different grounds in IPR2017-01884. Pet. 9; Paper 7, 2.

Patent Owner also identifies certain applications and patents that "claim or may claim the benefit of the priority of the filing date of [the '487 patent]." Paper 7, 1–2.

B. The ’487 Patent

The ’487 patent relates to compositions and methods for treating certain conditions induced by interleukin-4 (IL-4) by administering an IL-4 antagonist to a patient with such a condition. Ex. 1001, 3:9–14. IL-4 has a broad spectrum of biological activities, including growth of co-stimulation of T cells, mast cells, granulocytes, megakaryocytes, and erythrocytes. *Id.* at 1:29–36. IL-4 binds to specific cell surface receptors called interleukin-4 receptors (IL-4R). *Id.* at 1:49–51. Binding of IL-4 to IL-4R results in transduction of a biological signal to cells, such as various immune effector cells. *Id.* IL-4 has been implicated in a number of disorders, including allergy and asthma. *Id.* at 2:1–2, 4:11–31.

Different IL-4 antagonists may act at different sites or by different mechanisms of action. *Id.* at 10:47–48. According to the ’487 patent, examples include antagonists that interfere with binding of IL-4 to cell surface receptors or that inhibit signal transduction. *Id.* at 10:48–50. The site of action may be intracellular, on a cell surface, or extracellular. *Id.* at 10:50–53. Antagonists may bind to either IL-4 or to the receptor. *Id.* at 10:53–54. Examples of IL-4 antagonists include IL-4 receptors, antibodies that bind to IL-4 or IL-4R, other IL-4 binding molecules, and IL-4 muteins. *Id.* at 10:36–38.

Blocking antibodies that interfere with the binding of IL-4 to IL-4R may be raised against either IL-4 or IL-4R. The antibodies can be screened in conventional assays for their ability to interfere with binding of IL-4 to IL-4R. *Id.* at 18:40–45. Because it has been found that IL-4R is a component of certain multi-subunit IL-13 receptor complexes, some antibodies raised against IL-4R may interfere with the binding of IL-13 to those complexes. *Id.* at 18:50–57. Those antibodies may inhibit both IL-4

induced biological activity and IL-13 induced activity and therefore may be used in treating conditions induced by either or both cytokines. *Id.* at 18:58–62. Such conditions include IgE-mediated conditions, asthma, allergic conditions, allergic rhinitis, and dermatitis. *Id.* at 18:62–65.

The '487 patent identifies examples of IL-4R human monoclonal antibodies (MAbs) produced by immunizing transgenic mice. The examples are designated MAbs 6-2, 12B5, 63, 1B7, 5A1, and 27A1. *Id.* at 21:6–11. MAbs 12B5, 63, and 1B7 are preferred fully human antibodies capable of inhibiting activity of both IL-4 and IL-13. *Id.* at 21:11–15.

The '487 patent presents the encoded amino acid sequence of the variable region of the light chain MAb 12B5 in SEQ ID NO:10, and of the variable region of the heavy chain in SEQ ID NO:12. *Id.* at 22:36–41.

C. Illustrative Claim

Petitioner challenges claims 1–14, 16, and 17 of the '487 patent, of which claim 1 is the only independent claim. Claim 1 is illustrative and is reproduced below:

> 1. An isolated human antibody that competes with a reference antibody for binding to human IL-4 interleukin-4 (IL-4) receptor, wherein the light chain of said reference antibody comprises the amino acid sequence of SEQ ID NO:10 and the heavy chain of said reference antibody comprises the amino acid sequence of SEQ ID NO:12.

Ex. 1001, 77:26–31.

D. The Asserted Ground of Unpatentability

Petitioner contends that claims 1–14, 16, and 17 of the '487 patent are unpatentable as anticipated by the '132 Publication.[1] Petitioner relies on the Declaration of Gerard Zurawski, Ph.D. (Ex. 1200) to support its assertion.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art would have had at least a Ph.D. or an M.D. with research experience in immunology, biochemistry, cell biology, molecular biology, or a related field or at least 2–3 years of professional experience in one or more of those fields. Pet. 22–23. According to Petitioner, such a person would have had an understanding of "how one generates antibodies to a chosen antigen from animals (*e.g.*, mice), and how one isolates human antibodies by generating human antibodies directly from transgenic animals or transforming animal antibodies into human antibodies." *Id.* at 23 (citing Ex. 1200 ¶ 22). Patent Owner does not address the level of ordinary skill in the art in its Preliminary Response.

On this record, we adopt Petitioner's uncontested definition of the level of ordinary skill in the art. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not

[1] John D. Pluenneke, US 2002/0002132 A1, published Jan. 3, 2002 ("the '132 Publication," Ex. 1016).

shown") (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)).

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, and absent any special definitions, we generally give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

We determine that it is unnecessary to expressly construe any claim terms for purposes of this Decision.[2] *See Wellman, Inc. v. Eastman Chem.*

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[2] Patent Owner argues we should deny institution, as we did in IPR2017-01129, because Petitioner again fails to explain its inconsistent claim construction positions taken in district court litigation, including its assertion that 35 U.S.C. § 112, ¶ 6 should apply to the construction of "antibody." Prelim. Resp. 23–31. We decline to do so because the facts and circumstances of the -1129 proceeding differ from those here. For example, as Petitioner notes, even if "antibody" were limited to the six MAbs identified in the '487 patent, the '132 Publication discloses MAb 6-2, which is one of the six disclosed MAbs. Pet. 33–34 n.5. We note, however, that the better practice for the future would be to address such inconsistent positions, as institution is discretionary and other panels on differing facts might be less inclined to do so.

Co., 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc*., 200 F.3d 795, 803 (Fed. Cir. 1999)).

C. Whether to Exercise Our Discretion to Deny Institution

As an initial matter, Patent Owner argues that we should exercise our discretion under 35 U.S.C. §§ 314(a) or 325(d) to deny institution. For the reasons discussed below, we decline to do so under the facts of this case.

1. 35 U.S.C. § 314(a)

The Director has discretion whether to institute *inter partes* review under 35 U.S.C. § 314(a). *See* 35 U.S.C. § 314(a) (stating "[t]he Director *may not* authorize an inter partes review to be instituted . . . .") (emphasis added). As set forth in *General Plastic Industrial Co. v. Canon Kabushiki Kaisha*, IPR2016-01357 (PTAB Sept. 6, 2017) (Paper 19) (precedential), the Board has consistently considered a number of factors when determining whether to exercise that discretion. *Id.* at 15–16. Those seven factors include whether the same petitioner previously filed a petition directed to the same claims of the same patent, whether the petitioner knew of the prior art asserted in the second petition when filing the first petition, and whether at the time of filing the second petition, the petitioner already received the patent owner's preliminary response to the first petition. *Id.* at 16. We noted, however, that there is no *per se* rule precluding the filing of follow-on petitions and that the list of factors to consider is non-exhaustive. *See id.* at 15–16; *see also id.* at 18 ("We recognize that there may be circumstances where multiple petitions by the same petitioner against the same claims of a patent should be permitted, and that such a determination is dependent on the facts at issue in the case.").

The instant Petition represents Petitioner's second challenge to the claims of the '487 patent. Petitioner filed its first petition on March 23, 2017, in IPR2017-01129 challenging claims 1–17 of the '487 patent. In that petition, Petitioner argued the claims of the '487 patent were anticipated by the prior art because the claims were not entitled to the benefit of their earliest effective filing date. We denied institution, finding Petitioner had not sufficiently made that showing. IPR2017-01129, slip op. at 14 (PTAB Oct. 4, 2017) (Paper 19). Four months after filing its first petition, on July 28, 2017, Petitioner filed the instant Petition, asserting claims 1–14, 16, and 17 are anticipated under 35 U.S.C. § 102(e). Three days after that, on July 31, 2017, Petitioner filed a third petition in IPR2017-01884 ("IPR1884"), asserting claims 1–17 are unpatentable as obvious under 35 U.S.C. § 103.

Patent Owner argues that each of the seven *General Plastic* factors favors denial of the Petition. Prelim. Resp. 8–23. For example, it is undisputed that Petitioner previously challenged the same claims of the same patent; knew of the '132 Publication before filing the first petition; and had already received Patent Owner's preliminary response to the first petition at the time of filing this Petition (and responded to certain arguments in the instant Petition). Prelim. Resp. 8–14. Patent Owner also contends that Petitioner has failed to provide an adequate explanation for why it filed multiple petitions. *Id.* at 15–18.

In response, Petitioner asserts that the '487 patent does not specify how to determine whether an antibody "competes with a reference antibody," as required by the claims. Reply 4–5. According to Petitioner, it was not until November 23, 2016, in a European Patent Office proceeding, that Patent Owner endorsed two competition assays disclosed in the prior art as methods for determining competition. *Id.* at 5; Ex. 1201, 12–13.

Petitioner explains that it then "identified and retained experts, prepared the relevant antibodies, and conducted experiments demonstrating that mAb 6-2 'competes' and anticipates the claims. These experiments were complete on July 19, 2017, and the instant Petition was filed only seven business days later." Reply 5; Ex. 1200 ¶ 81.

Having considered each of the *General Plastic* factors and the facts and circumstances of this case, under the unique facts of this case we are not inclined to exercise our discretion to deny the Petition under § 314(a). We are persuaded that the grounds are sufficiently different in each petition that Petitioner did not appear to "strategically stage [its] prior art and arguments in multiple petitions, using [Patent Owner's preliminary response] as a roadmap, until a ground is found that results in the grant of review." *See General Plastic*, IPR2016-01357, slip op. at 17. We are also persuaded that the delayed filing of the latter two petitions to allow time for Petitioner to complete the competition assay testing was reasonable, particularly because it was not an issue in the first petition.

2. 35 U.S.C. § 325(d)

The Director also has discretion to decline to institute *inter partes* review if "the same or substantially the same prior art or arguments previously were presented to the Office." 35 U.S.C. § 325(d). Patent Owner argues that the Office already considered art containing the same allegedly anticipatory disclosures in the '132 Publication during prosecution of the '487 patent application. Prelim. Resp. 31–35. The Examiner identified March[3] and stated "[t]he art made of record and not relied upon is considered pertinent to applicant's disclosure." Ex. 1002, 51.

[3] March et al., US 2002/0076409 A1, published June 20, 2002 (Ex. 1202).

Petitioner notes that during prosecution, Patent Owner repeatedly argued that the Examiner had to provide evidence that the prior art antibodies compete with the '487 patent's reference antibody to maintain the anticipation rejection. Pet. 27–29; *see, e.g.*, Ex. 1002, 75–76 ("[I]t cannot be concluded that an antibody made according to [the asserted prior art] would *necessarily* compete for binding with the reference antibody of the rejected claims. Should this rejection be maintained, however, Applicants respectfully request that either documentary evidence . . . or an affidavit or declaration . . . supporting the assumption be provided."). Thus, Petitioner argues that the Board should not exercise its discretion under § 325(d) because the Office lacked the evidence submitted by Petitioner in this proceeding that the prior art anti-IL-4R antibodies practice the "competes" limitation. Reply 4.

Having considered the arguments and evidence of both parties, we are persuaded that Petitioner has the better position. Because the Examiner did not have the benefit of Petitioner's additional experimental evidence relating to competition, we are not persuaded that the same or substantially the same prior art or arguments were previously presented to the Office. Nor was the evidence contained in Dr. Zurawski's declaration before the Examiner. Accordingly, under the facts and circumstances of this case, we decline to exercise our discretion to deny institution under § 325(d).

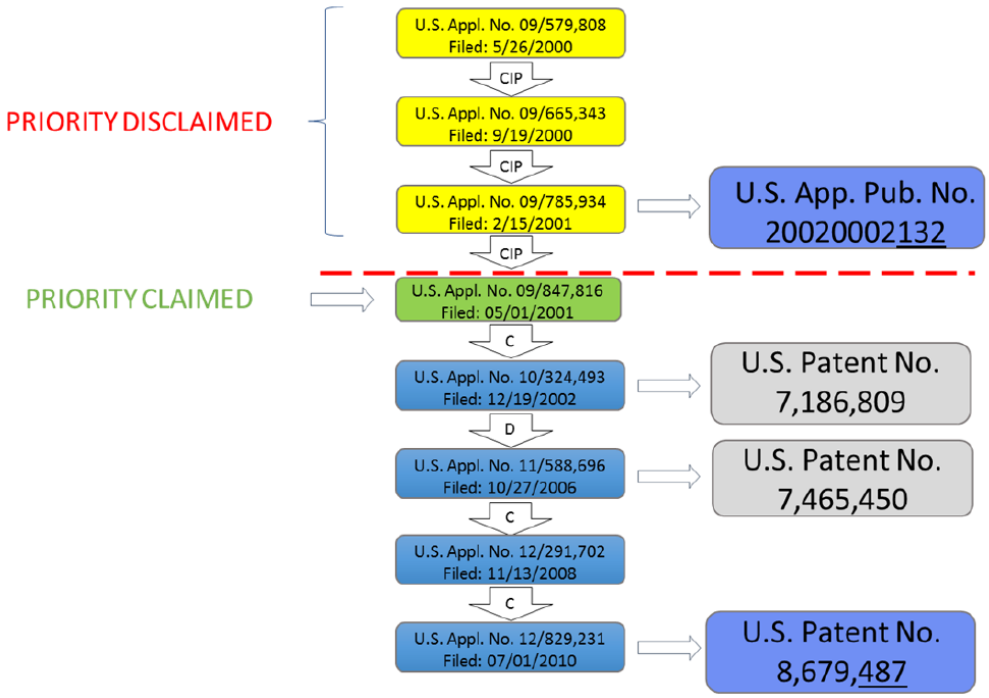
D. Anticipation by the '132 Publication

Petitioner asserts that claims 1–14, 16, and 17 of the '487 patent are anticipated by the '132 Publication. Pet. 40–61. Patent Owner opposes Petitioner's assertion. Prelim. Resp. 9–57. On this record, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the challenged claims are anticipated by the '132 Publication.

1. The '132 Publication (Ex. 1016)

The '132 Publication, entitled "Use of Interleukin-4 Antagonists and Compositions Thereof," identifies John D. Pluenneke as the sole inventor and is the publication of U.S. Application No. 09/785,934 ("the '934 application"). Ex.1016, [21], [54], [76]. The '934 application is the parent of U.S. Application No. 09/847,816, to which the '487 patent claims priority. Ex. 1001, [60]. Patent Owner, however, expressly disclaimed priority to the '132 Publication (and the earlier applications) during prosecution of the '487 patent. Ex. 1002, 145.

Petitioner provides an illustration, reproduced below, of the chain of applications leading to the '487 patent, including the disclaimed applications:



Pet. 3. The illustration shows the '816 application is a continuation-in-part of the '132 Publication. Thus, the disclosure of the '132 Publication is a subset of that of the '487 patent. *See* Ex. 1203 (redline comparison of the

disclosures of the ’132 Publication with the ’487 patent). For example, the ’487 patent adds a portion of Example 6, all of Examples 8 and 9, and the disclosure of SEQ ID NOS: 4–26. Pet. 37 n.6.

In particular, the ’132 Publication discloses as Example 6 a hybridoma cell line designated “6-2” that secretes mAb 6-2. Ex. 1016 ¶ 246. Paragraph 246 states:

> One hybridoma cell line generated by procedures described above (see example 4) is designated 6-2. The anti-IL-4R monoclonal antibody secreted by this hybridoma is a blocking antibody, as determined in a conventional plate binding assay, and thus functions as an IL-4 antagonist. The monoclonal antibody produced by 6-2 also exhibits the ability to reduce an IL-13-induced biological activity.

Id.

2. Analysis

Anticipation requires that “each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (citation omitted). “To establish inherency, the extrinsic evidence ‘must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.’” *Id.* (citation omitted).

Regarding claim 1, Petitioner asserts that the ’132 Publication discloses, expressly or inherently, each limitation of the claim. For example, Petitioner contends that the ’132 Publication’s teaching of mAb 6-2, which was isolated and screened according to Examples 4–6, discloses “an isolated human antibody.” Pet. 40–42 (citing Ex. 1016 ¶¶ 232–241, 243, 246); Ex. 1200 ¶¶ 123–127. Petitioner further contends that the mAb 6-2 antibody of the ’132 Publication inherently “competes with a reference antibody for

binding to human IL-4 interleukin (IL-4) receptor, wherein the light chain of said reference antibody comprises the amino acid sequence of SEQ ID NO:10 and the heavy chain of said reference antibody comprises the amino acid sequence of SEQ ID NO:12." *Id.* at 43–49; Ex. 1200 ¶¶ 128–129. Specifically, Petitioner's declarant, Dr. Zurawski, testifies that he confirmed experimentally that the mAb 6-2 antibody competes with the claimed reference antibody (mAb 12B5). Ex. 1200 ¶¶ 79–106. Dr. Zurawski states that he used the competition assay described in Perez de la Lastra (1999), which was endorsed by Patent Owner during a European Opposition proceeding. *Id.* ¶ 97.

On this factual record, we are persuaded that Petitioner has shown sufficiently that the '132 Publication discloses each limitation of claim 1. We have considered the arguments and evidence with respect to claims 2–14, 16, and 17, and we are persuaded that Petitioner has made a sufficient showing as to those claims, as well. *See* Pet. 49–61; Ex. 1200 ¶¶ 130–179.

At this stage of the proceeding, Patent Owner does not dispute that the '132 Publication discloses each limitation of the claims, expressly or inherently. Instead, Patent Owner argues the Petition fails to show the '132 Publication enables a person of ordinary skill in the art to make the 6-2 antibody. Prelim. Resp. 35–38. The Petition states that the '132 Publication "discloses how the 6-2 antibody was made, screened, and tested." Pet. 38–39. According to Petitioner, this includes:

> (1) disclosure of the generation of transgenic mice in Example 3 (Ex. 1016 ['132 Publication] at ¶¶ [0232]–[0236]; (2) disclosure of how to generate and screen for anti-hIL-4R mAbs like mAb 6-2 from transgenic mice as shown in Examples 1 and 4 (Ex. 1016 ['132 Publication] at ¶¶ 0218–0220, [0237]–[0241]); and (3) disclosure of how to assay generated antibodies like mAb 6-

> 2 for IL=4 and IL-13 blocking activity as described in Example 5 (Ex. 1016 ['132 Publication] at ¶¶ [0237]–[0241]).

Id. at 38.

Patent Owner argues that the Petition, at best, asserts that the '132 Publication would have enabled a person of ordinary skill in the art how to make antibodies "*like mAb 6-2*." Prelim. Resp. 36. According to Patent Owner, the Petition does not enable how to make the 6-2 antibody, specifically, as evidenced by Dr. Zurawski's need to rely on the sequence information disclosed in the '487 patent to prepare the 6-2 antibody. *Id.* at 37–38 (citing *Elan Pharms. v. Mayo Found.*, 346 F.3d 1051, 1054 (Fed. Cir. 2003) ("To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to *make the anticipating subject matter*.") (emphasis added)).

Patent Owner also argues that the relied-upon portions of the '132 Publication do not describe an invention "by another," and are therefore not prior art under 35 U.S.C. § 102(e). *Id.* at 38–60. Patent Owner provides documentary and testimonial evidence, including the testimony of each '487 patent inventor and two research associates, stating the relied-upon portions of the '132 Publication represent the joint work of the '487 patent inventors and not the work of the listed inventor of the '132 Publication, John D. Pluenneke. *Id.* at 42–43. Patent Owner also provides a declaration from Mr. Pluenneke stating the relied-upon portions of the '132 Publication "do not reflect my work." Ex. 2011 ¶ 8.

Having considered the arguments and evidence, it appears a threshold issue in dispute in this proceeding is whether the '132 Publication constitutes § 102(e) prior art. In *Dynamic Drinkware, LLC v. National Graphics, Inc.*, 800 F.3d 1375 (Fed. Cir. 2015), the Federal Circuit explained the shifting

burden of production with respect to showing whether a reference is prior art. *Id.* at 1379–80. Although the burden of persuasion never shifts to Patent Owner, Petitioner has satisfied its initial burden of production by arguing that the '132 Publication anticipates the challenged claims under § 102(e). *See id.* at 1379 (stating the petitioner satisfied its initial burden of production by arguing that the prior art anticipated the claims under § 102(e)(2)). The burden of production then shifts to Patent Owner to argue or produce evidence that the '132 Publication does not anticipate or that the '132 Publication is not prior art. Having argued that the '132 Publication is not prior art because it is not enabling and is not work "by another," the burden of production shifts back to Petitioner to prove that the '132 Publication actually anticipates and constitutes prior art under § 102(e). *See id.* at 1380.

Although we find the evidence and arguments presented by Patent Owner compelling, we are not prepared, on this record, to foreclose Petitioner the opportunity to respond to Patent Owner's arguments and the disputed issues of fact regarding whether the '132 Publication constitutes § 102(e) prior art. *See* 37 C.F.R. § 42.108(c) ("The Board's decision [whether to institute] will take into account a patent owner preliminary response . . ., including any testimonial evidence, but a genuine issue of material fact created by such testimonial evidence will be viewed in the light most favorable to the petitioner solely for purposes of deciding whether to institute an *inter partes* review."). At this stage of the proceeding, we find that Petitioner has offered sufficient evidence to institute trial. That being said, we will be able to evaluate both parties' arguments and evidence more thoroughly once the record is developed further during trial.

Accordingly, having considered the arguments and evidence, we are persuaded that Petitioner has shown a reasonable likelihood that it would prevail in its assertion that claims 1–14, 16, and 17 are anticipated by the ’132 Publication.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has established a reasonable likelihood of prevailing on its assertion that claims 1–14, 16, and 17 of the ’487 patent are unpatentable.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on the following ground:

Claims 1–14, 16, and 17 as anticipated by the ’132 Publication.

FURTHER ORDERED that no other proposed grounds of unpatentability are authorized.

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this decision.

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