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Paper No. 16
Date: June 17, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GEMOAB MONOCLONALS GMBH,
Petitioner,

v.

UNIVERSITY OF MARYLAND, BALTIMORE,
Patent Owner.

IPR2020-00233
Patent 9,233,125 B2

Before JON B. TORNQUIST, TINA E. HULSE, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

GEMoaB Monoclonals, GmbH ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–21 of U.S. Patent No. 9,233,125 B2 (Ex. 1001, "the '125 patent"). Paper 2 ("Petition" or "Pet."). University of Maryland, Baltimore ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp.").

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) (2018). Upon considering the argument and evidence presented in the Petition and Preliminary Response, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition. Accordingly, we decline to institute an *inter partes* review of any claim of the '125 patent on any ground.

A. Real Parties-in-Interest

Petitioner identifies itself, GEDAD Beteiligungs- und Verwaltungs-GmbH, Cellex Gessellschaft für Zellgewinnung mbG, CPT Cellex Patient Treatment GmbH, and CMT Cellex Manufacturing Transports and Logistics GmbH as real parties-in-interest. Pet. 69.

Patent Owner identifies itself, Living Pharma, Inc., Lentigen Technology, Inc., Miltenyi Biotec B.V. & Co. KG, Miltenyi Biotec, Inc., Miltenyi Biotec, North America, Inc., Miltenyi Biotec GmbH, Miltenyi Biotec Technology, Inc., Owl Biomedical, Inc., and LaVision Biotech GmbH as real parties-in-interest. Paper 4, 1.

B. Related Proceedings

The parties state there are no related judicial or administrative matters. Pet. 69; Paper 4, 1. The parties also identify U.S. Patent Application No. 14/990,514, which claims the benefit of priority to the '125 patent. Pet. 70, Paper 4, 1.

C. The '125 Patent

The '125 patent relates to T cell-based anti-cancer therapeutics and methods of using the therapeutics to treat cancer. Ex. 1001, 1:16–18. One strategy for T cell-based therapies involves the use of genetic engineering to express a chimeric antigen receptor (CAR) on T cells. *Id.* at 1:25–27. The extracellular domain of a typical CAR consists of a single-chain fragment variable (scFv) from the antigen binding sites of a monoclonal antibody. *Id.* at 1:27–30. The scFv is linked to a flexible transmembrane domain followed by a tyrosine-based activation motif. *Id.* at 1:30–32. CAR T cells seek out and kill cancer cells by recognizing tumor-associated antigens (TAA) expressed on their surface. *Id.* at 1:38–41. Various early-phase trials have demonstrated the efficacy of CAR T cells to treat cancer patients with solid tumors and hematopoietic malignancies. *Id.* at 1:43–46.

Although various early-phase trials of CAR T cells have been promising, there are several limitations to their generalized clinical application. *Id.* at 1:51–53. For example, because no single tumor antigen is universally expressed by all cancer types, scFVs must be constructed for each tumor antigen targeted, which is both costly and labor intensive. *Id.* at 1:53–59. Moreover, tumor antigens targeted by CARs may be downregulated or mutated, which would negate the therapeutic effects of CAR T cells, which recognize only one target antigen. *Id.* at 1:59–63.

Finally, CAR T cells react with target antigen weakly expressed on non-tumor cells, which may cause severe adverse effects. *Id.* at 1:65–67.

To address the deficiencies of CAR T cell systems, the '125 patent describes "a universal, yet adaptable, anti-tag chimeric antigen receptor (AT-CAR) system which provides T cells with the ability and specificity to recognize and kill target cells, such as tumor cells, that have been marked by tagged antibodies." *Id.*, Abstract. In one embodiment, αFITC-CAR-expressing human T cells specifically recognize various human cancer cells when those cells are bound by cancer-reactive FITC-labeled antibodies.[1] *Id.* at 2:23–26. The activation of the αFITC-CAR T cells induces target cell lysis, T cell proliferation, and cytokine/chemokine production in vitro and ex vivo. *Id.* at 2:27–29. According to the specification, "[t]his 'off-the-shelf' system advances existing CAR technology through its potential to target various tagged proteins in the treatment of cancer patients." *Id.* at 2:36–38.

D. Illustrative Claims

Petitioner challenges claims 1–21 of the '125 patent, of which claims 1–3 are independent. Claim 1 is illustrative and is reproduced below.

> 1. A method of treating cancer in a subject, comprising:
>
> (a) administering a formulation of tagged proteins to a subject in need of treatment, wherein the tagged proteins bind a cancer cell in the subject, and
>
> (b) administering a therapeutically-effective population of anti-tag chimeric receptor (AT-CAR)-expressing T cells to the subject, wherein the AT-CAR-expressing T cells bind the tagged proteins and induce cancer cell death, thereby treating cancer in a subject.

Ex. 1001, 19:38–46.

[1] Fluorescein isothiocyanate (FITC) is a fluorophore that can be detected using flow cytometry or fluorescence microscopy. Ex. 1002 ¶ 34.

Independent claim 2 is identical to claim 1 but recites administering "one or more" formulations of tagged proteins and therapeutically-effective populations of AT-CAR-expressing T cells. *Id.* at 19:47–56. Similarly, independent claim 3 recites administering "at least two" formulations of tagged proteins and therapeutically-effective populations of AT-CAR-expressing T cells, but is otherwise identical to claim 1. *Id.* at 19:57–65.

Dependent claims 4–21 depend either directly or indirectly from claim 1. Claims 4–6 further limit the structure of the tagged proteins; claims 7–13 further limit the structure of the AT-CAR of the AT-CAR-expressing T cells; claims 14 and 15 further limit the source of the T cells; claims 16–19 further limit the order of administering the tagged proteins and the population of therapeutically effective AT-CAR-expressing T cells; claim 20 recites inducing cytolytic activation of the T cells when bound to tagged proteins that are bound to a cancer cell; and claim 21 recites that the subject is human. *Id.* at 19:66–21:32.

E. The Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–21 would have been unpatentable on the following grounds:

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1–5, 7–13, 16–21	102[2]	UPenn[3]
1–13, 16–21	103	UPenn
1, 2, 4, 5, 7–11, 13	102	Ang[4]
1–11, 13, 20, 21	103	Ang
12, 16–19	103	Ang, UPenn
14, 15	103	UPenn, Itoh[5]
14, 15	103	Ang, Itoh

Petitioner also relies on the Declaration of Roderick O'Connor, Ph.D. Ex. 1002.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art at the time of the invention (either December 2010 or December 2011) would have had "at

[2] Because the claims at issue have an effective filing date before March 16, 2013, the effective date of the applicable provisions of the Leahy Smith America Invents Act, Pub. L. No. 112–29, 125 Stat. 284 (2011) ("AIA"), we apply the pre-AIA versions of 35 U.S.C. §§ 102, 103(a) and 112 in this Decision.

[3] Scholler, et al., WO 2013/044225 A1, published Mar. 28, 2013 ("UPenn," Ex. 1008).

[4] Ang, et al., *Generating a Chimeric Antigen Receptor to Redirect T-Cell Specificity* after *Infusion*, 19 MOLECULAR THERAPY Supp. 1 S137 (2011) ("Ang," Ex. 1006).

[5] Kyogo Itoh, US 2003/0175288 A1, published Sept. 18, 2003 ("Itoh," Ex. 1039).

least a Ph.D. in the field of immunology, biochemistry, cell biology, molecular biology, molecular pharmacology, or a related field and at least 2 years of experience in the field of CAR-T cells." Pet. 23 (citing Ex. 1002 ¶ 14). Patent Owner does not contest Petitioner's definition of the person of ordinary skill in the Preliminary Response. *See generally* Prelim. Resp.

At this stage of the proceeding, and without opposition from Patent Owner, we apply Petitioner's definition because it is consistent with the level of skill in the art at the time of the invention as reflected by the prior art and the disclosure of the '125 patent. *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 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 applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 42.100(b) (2019). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at

1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

Petitioner offers proposed claim constructions for the terms "tagged protein" and "AT-CAR"/"anti-tag chimeric receptor." Pet. 24–25. Patent Owner disputes Petitioner's proposed construction of "tagged proteins." Prelim. Resp. 36–42. For purposes of this Decision, we need only address the construction of "tagged proteins." *See Wellman, Inc. v. Eastman Chem. 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))).

Each of the '125 patent claims recites administering "tagged proteins" to a subject. The parties' claim construction dispute centers around the scope of the term "proteins." Petitioner asserts that the term "protein" "broadly encompasses any type of molecule that serves the required function." Pet. 24. As support, Petitioner cites the '125 patent specification:

> The tagged proteins bind to target cells in the subject. In general, the 'protein' portion of the tagged protein is the portion of the molecule that binds to the target cell. For example, the protein may be an antibody that binds to a tumor associated antigen (TAA) or a tumor specific antigen (TSA) expressed by the target cell. However, ***the 'protein' may be any molecule that binds to a target cell.***

Ex. 1001, 9:37–43 (emphasis added by Petitioner). Thus, according to Petitioner, the term "protein" encompasses molecules that are not proteins as long as they bind to a target cell.

Patent Owner disagrees. According to Patent Owner, Petitioner's construction is inconsistent with the plain, ordinary meaning of "protein," expands the scope of "protein" beyond the scope described in the '125 patent specification, and is untethered to any definitional language in the specification that could change the ordinary meaning. Prelim. Resp. 37.

We find Patent Owner has the better position. We agree that the plain, ordinary meaning of the term "protein" is a molecule composed of amino acids. *See* Ex. 2005, 124. Petitioner's proposed construction is broader than the plain, ordinary meaning of "protein," as it includes molecules that are not proteins. Any special definitions for claim terms, however, must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994). We do not read the '125 patent specification as redefining "proteins" to include molecules that are not actually proteins. Rather, we find the portion of the '125 patent specification cited by Petitioner to be taken out of context. When the specification states "the 'protein' may be any molecule that binds to a target cell," Ex. 1001, 9:42–43, we interpret that to mean any *protein* molecule that binds to a target cell, as the term "protein" itself identifies the molecule as a protein molecule.

The examples of the specification support our interpretation. The specification identifies several exemplary proteins that are anti-cancer-based monoclonal antibodies. *Id.* at 9:43–50. But the specification also identifies other examples of tagged proteins. The specification states "T cells expressing αFITC-VEGF as the AT-CAR can target endothelial vascular cells to which FITC-tagged VEGF is bound, where the FITC-tagged VEGF is bound by the VEGF receptor." *Id.* at 10:11–14. Thus, the specification describes FITC-tagged vascular endothelial growth factor as an example of a

tagged protein that is not an antibody. In contrast, Petitioner cites no examples of tagged proteins that are not actually proteins.

Moreover, construing the term "tagged protein" as "a molecule that includes a portion that binds to the cancer cell and a portion that can be recognized and specifically bound by the AT-CAR" is unnecessary, as those functions are already defined by the claim language itself. That is, each of the independent claims already recites "wherein the tagged proteins bind a cancer cell" and "wherein the AT-CAR-expressing T cells bind the tagged proteins." *E.g.*, *id.* at 19:40–41, 44–45 (claim 1). Construing the term "tagged proteins" as proposed by Petitioner "ascribes no meaning to the term . . . not already implicit in the rest of the claim." *See Mangosoft, Inc. v. Oracle Corp.*, 525 F.3d 1327, 1330–31 (Fed. Cir. 2008).

Having considered the parties' respective arguments and evidence, we find the '125 patent specification does not set forth a special definition for the term "tagged protein" beyond the plain, ordinary meaning of the term. Thus, we conclude that the term "tagged protein" is a tagged molecule composed of amino acids, i.e., a protein.

C. Effective Filing Date of the '125 Patent

The '125 patent was filed on December 14, 2011, and claims priority to Provisional Application No. 61/422,681 ("the 2010 Provisional"), which was filed on December 14, 2010. Ex. 1001, at [22], [60]. Petitioner contends that the '125 patent is not entitled to the benefit of the filing date of the 2010 Provisional, because the 2010 Provisional does not adequately describe or enable the claimed invention. Pet. 26–38. Patent Owner disagrees. Prelim. Resp. 35–62.

We consider this dispositive issue first, because if we apply the 2010 Provisional's December 14, 2010, filing date as the earliest effective filing

date of the '125 patent, neither UPenn nor Ang qualifies as prior art, which is fatal to each ground in the Petition.

1. Legal Background

For a patent to claim the benefit of the filing date of its provisional application, the specification of the provisional "must 'contain a written description of the invention and the manner and process of making and using it, in such full, clear, concise, and exact terms,' 35 U.S.C. § 112 ¶ 1, to enable an ordinarily skilled artisan to practice the invention claimed in the non-provisional application." *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (emphases omitted) (quoting *New Railhead Mfg., L.L.C. v. Vermeer Mfg. Co.*, 298 F.3d 1290, 1294 (Fed. Cir. 2002)); *see also* 35 U.S.C. § 119(e)(1).

In evaluating the effective filing date of the '125 patent to determine whether to institute an *inter partes* review, we first address the parties' respective burdens. In an *inter partes* review, Petitioner bears the ultimate burden of persuasion regarding unpatentability, which never shifts to patent owner. *Dynamic Drinkware*, 800 F.3d at 1379. But *Dynamic Drinkware* also establishes that Petitioner has the initial burden of production to show a reference is prior art. *Dynamic Drinkware*, 800 F.3d at 1379. The burden of production then shifts to Patent Owner to refute Petitioner's argument by either showing the prior art does not actually render the claims unpatentable or does not qualify as prior art. *Id.* at 1380. The burden of production then shifts back to Petitioner to respond to Patent Owner's argument. *Id.* The Board then evaluates all of the evidence and determines whether Petitioner has satisfied its burden of persuasion regarding unpatentability. *Id.*

At institution, the Board has applied a similar burden-shifting approach with respect to the effective filing date of the challenged claims.

Our colleagues in *Polaris Wireless, Inc. v. TruePosition, Inc.*, IPR2013-00323, Paper 9 (PTAB Nov. 15, 2013) (Decision on Institution) explained the framework we apply here:

> In an *inter partes* review, the burden is on Petitioner to show a reasonable likelihood that it would prevail on a ground of unpatentability. With respect to entitlement to earlier effective filing dates, the Patent Owner is not presumed to be entitled to the earlier filing dates of ancestral applications which do not share the same disclosure. But, the issue first has to be raised by Petitioner in its petition, by identifying, specifically, the features, claims, and ancestral applications allegedly lacking § 112, first paragraph, written description and enabling disclosure support for the claims based on the identified features. Then, the Patent Owner has to make a sufficient showing of entitlement to earlier filing date or dates, in a manner that is commensurate in scope with the specific points and contentions raised by Petitioner.

Id. at 29. In other words, because the 2010 Provisional does not have the same disclosure as the '125 patent, we do not presume the '125 patent is entitled to the benefit of the 2010 Provisional's filing date. But because Petitioner has the burden to show a reasonable likelihood of prevailing on a ground of patentability to institute trial, we require Petitioner to first identify *with specificity* the limitations of the '125 patent claims that it asserts lack written description and enabling support in the 2010 Provisional. The burden of production then shifts to Patent Owner to respond to Petitioner's specific arguments to show sufficiently that the '125 patent claims are entitled to the earlier filing date of the 2010 Provisional.

This approach has been repeatedly applied by our colleagues at the institution phase. *See, e.g.*, *Huawei Techs. Co. v. Samsung Elecs. Co.*, IPR2017-01980, Paper 9 at 9–10 (PTAB Feb. 27, 2018) (discussing *Dynamic Drinkware*); *Franklin Elec. Co. v. Liberty Pumps, Inc.*, IPR2017-00113, Paper 14 at 12–13 (PTAB Apr. 27, 2017) (same); *Lupin Ltd. v. Pozen*

Inc., IPR2015-01775, Paper 15 at 10–11 (PTAB Mar. 1, 2016). We therefore apply this framework when considering whether the parties have met their respective burdens at this stage of the proceeding.

2. Whether the 2010 Provisional Describes the Claimed Invention

To show sufficient written description under 35 U.S.C. § 112 ¶ 1, "the description must 'clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'" *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (quoting *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991)). Stated differently, the disclosure must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.*

Petitioner asserts the 2010 Provisional fails to adequately describe the claimed invention because the inventors of the '125 patent were not in possession of the broad scope of the claims at the time of the 2010 Provisional. Pet. 27. Petitioner's argument is based on its proposed construction of "tagged protein," which "encompasses *any* molecule—not just a protein—that includes a portion that binds to the cancer cell and a portion that can be recognized and specifically bound by the AT-CAR." *Id.* at 28. Petitioner also asserts that the specification states the term "tag" "is only constrained by being a molecular [sic] that can be recognized and specifically bound by the AT-CAR, specifically the tag-binding domain of the AT-CAR." *Id.* (citing Ex. 1001, 9:51–54). Given the "broad and generic" construction of "tagged proteins," Petitioner asserts the 2010 Provisional does not provide sufficient written description support for the full scope of the claim. *Id.* (citing *Ariad*, 598 F.3d at 1350). That is, Petitioner asserts the 2010 Provisional lists only fourteen prophetic tags and

only proposes conjugating them to a peptide or protein, such as an antibody. *Id.* According to Petitioner, the 2010 Provisional does not contemplate the use of any other tags or tagged proteins that are not peptide or protein based. *Id.*

In response, Patent Owner argues Petitioner's written description argument fails because it is based on an improper claim construction. Prelim. Resp. 42 (citing *Intirtool, Ltd. v. Texar Corp.*, 369 F.3d 1289, 1296 (Fed. Cir. 2004) (holding the district court's reliance on an erroneous claim construction as the basis for its written description finding to be clearly erroneous)).

We agree with Patent Owner. As explained above, we do not construe the term "tagged proteins" to encompass molecules that are not proteins. Rather, we construe "tagged proteins" mean protein molecules that are tagged, which, as Patent Owner notes, are described in the 2010 Provisional. *See* Prelim. Resp. 47 (citing, e.g., Ex. 1004, 2 ("A tag is conjugated to a peptide or protein which exhibits high affinity to one or more molecules expressed on the target tissue cell.")).

Thus, on this record, we find Patent Owner has made a sufficient showing that the 2010 Provisional provides written description support for the "tagged proteins" of the '125 patent claims, when properly construed.

3. Whether the 2010 Provisional Enables the Claimed Invention

Under 35 U.S.C. § 112 ¶ 1, the specification must enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). To determine whether undue experimentation would be required, we may consider the following "*Wands* factors": (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.*

Because Petitioner has the initial burden to specifically identify how the 2010 Provisional fails to enable the claims, we address the *Wands* factors in the order set forth by the Petition. *See* Pet. 30–34

a) The relative skill of those in the art

Petitioner defines a person of ordinary skill in the art as someone who would have had "at least a Ph.D. in the field of immunology, biochemistry, cell biology, molecular biology, molecular pharmacology, or a related field and at least 2 years of experience in the field of CAR-T cells." Pet. 23. Petitioner also notes a person of ordinary skill in the art is "highly skilled." *Id.* at 33. We agree and find this factor weighs in favor of enablement.

b) The breadth of the claims and the nature of the invention

Petitioner asserts the breadth of the claims and nature of the invention weigh in favor of a determination that undue experimentation would be required because the '125 patent broadly claims "tagged proteins" and the "potential combinations of tagged proteins, AT-CARs and cancer cells are effectively limitless." Pet. 30 (citing Ex. 1002 ¶ 84).

Patent Owner asserts Petitioner's argument should be rejected because it relies on Petitioner's overly broad claim construction of "tagged proteins." Prelim. Resp. 49. Patent Owner also asserts the 2010 Provisional "did not purport to invent proteins, tagged proteins, nor the use of CAR T cells to combat cancer." *Id.* at 50. Rather, Patent Owner asserts the 2010 Provisional "was merely adapting known technology and methods in a new way." *Id.* at 50.

We agree with Patent Owner. Like its written description argument, we find Petitioner's "breadth of claim" argument is unpersuasive because it relies on an overly broad construction of "tagged proteins." Furthermore, on this record, we are persuaded by Patent Owner's argument that the nature of the invention weighs in favor of enablement, as the claims adapt known technology and methods in a new way. *See, e.g.*, Ex. 1004, 2 ("The universal ATCAR provides a more efficient process than current Chimeric-Antigen-Receptor approaches.").

c) The amount of direction or guidance presented and the presence or absence of working examples

Petitioner asserts the 2010 Provisional provides no data, no working examples, and minimal guidance regarding the structure of the AT-CAR system. Pet. 31. Petitioner asserts the 2010 Provisional describes the method using prophetic language and provides no explanation of how a person of ordinary skill in the art would successfully use tagged proteins. *Id.* (citing Ex. 1002 ¶ 85). Specifically, Petitioner asserts that "[t]here is no explanation whatsoever as to *how* one might successfully accomplish this conjugation [of a tag to a peptide], what constitutes 'high affinity,' or how to determine what tags might be suitable." *Id.* (citing Ex. 1002 ¶ 85). Thus, Petitioner asserts these factors weigh strongly in favor of undue experimentation.

In response, Patent Owner asserts the Petition fails to consider what a person of ordinary skill in the art knew as of 2010. Prelim. Resp. 51; *see also id.* at 45–47. For example, Patent Owner asserts that as of at least 1995, a skilled artisan knew how to genetically engineer proteins, such as high-affinity antibodies. *Id.* at 45 (citing Ex. 2006, 36–38). Patent Owner also asserts that the Petition and Petitioner's expert admit that tagging antibodies

and producing targeted immune receptors such as CARs was well known. *Id.* at 46 (citing Pet. 6–7; Ex. 1002 ¶ 62 (citing Ex. 1037, a review article on using CAR-T cells for cancer immunotherapy submitted for publication in 2009)). Moreover, Patent Owner notes, the 2010 Provisional discloses fourteen tags that can be conjugated to a peptide or protein for which there are already known antibodies against. *Id.* at 53; Ex. 1004, 4 (Table 1). Given the knowledge of a skilled artisan and the disclosure of suitable tags, Patent Owner asserts the 2010 Provisional provides adequate guidance for how to make and use the claimed tagged proteins. Prelim. Resp. 53.

On this record, we find Patent Owner's argument persuasive. Petitioner does not appear to consider the knowledge of a person of ordinary skill in the art in evaluating the amount of guidance needed to enable the claimed invention. And, as our reviewing court states, "[a] patent need not teach, and preferably omits, what is well known in the art." *Falkner v. Inglis*, 448 F.3d 1357, 1365 (Fed. Cir. 2006) (citation omitted). As Patent Owner asserts, both Petitioner and its expert appear to agree that a person of ordinary skill in the art would have known how to genetically engineer high-affinity antibodies, how to tag antibodies, and how to produce CARs. *See* Prelim. Resp. 45–47. Although the 2010 Provisional does not provide a specific working example of the claimed invention, we are not persuaded on this record that that necessarily weighs heavily in favor of undue experimentation given the knowledge in the art and the disclosure of fourteen tags that were known to link to proteins for which known antibodies existed.

d) The state of the prior art and the predictability or unpredictability of the art

Petitioner asserts that at the time of the 2010 Provisional, universal CAR systems were a nascent technology and modifying the distance between the T cell and cancer cells would cause unpredictable results. Pet. 31–32 (citing Ex. 1002 ¶¶ 51–56, 86–92). Petitioner also asserts that during prosecution of a continuation application of the '125 patent, Patent Owner conceded that the art was unpredictable. *Id.* at 32 (citing Ex. 1057, 8–10; Ex. 1060, 8–10). Specifically, in an office action response to an obviousness rejection, Patent Owner submitted the Declaration of Dr. Andrew Kaiser, who stated that a person of ordinary skill in the art "would have doubted that proper activation of T cell cytolytic activity could be achieved when an additional, non-covalently bound spacer molecule, *i.e.* a tagged antibody, is inserted between the antigen expressed by a target cell and the chimeric receptor." Ex. 1005 ¶ 3. Thus, Petitioner asserts the nascent state of the art and the unpredictability of the art weigh in favor of undue experimentation.

In response, Patent Owner asserts that its prior statements about obviousness during prosecution of a different patent application are irrelevant to the issue of whether the 2010 Provisional enables the claimed invention. *Id.* at 55–56.

We agree with Patent Owner that obviousness and enablement are different issues. As explained by the Federal Circuit:

> The obviousness inquiry turns on what the prior art would have taught a person of ordinary skill in the art and whether the claimed invention would have been obvious in view of the *prior art*. . . . In contrast, the enablement inquiry turns on whether the skilled artisan, after reading the specification, would be able to

> make and use the claimed invention without undue experimentation, based on the ordinary skill in the art.

Allergan, Inc. v. Sandoz Inc., 796 F.3d 1293, 1310 (Fed. Cir. 2015). Thus, we do not find Dr. Kaiser's statements related to the reasonable expectation of success in light of the prior art to be dispositive of whether a person of ordinary skill in the art having read the 2010 Provisional could make and use the claimed invention without undue experimentation.

Nevertheless, we find that Dr. Kaiser's declaration testimony is consistent with Petitioner's and its expert's assertion that it was known in 2010 that the distance between a T cell and a target cell is an important factor in T cell activation. Pet. 11–12; Ex. 1002 (Dr. O'Connor) ¶ 52 ("The prevailing theory in 2010, which remains prevalent today, was known as the kinetic segregation model."); Ex. 1005 (Dr. Kaiser) ¶ 2 ("My opinion is based on the premise that the distances between the CAR-expressing cell and the antigen-expressing cells would likely shift due to the inclusion of an anti-tag antibody (or tag-binding portion thereof) in the system."). Thus, we find Petitioner has shown sufficiently at this stage of the proceeding that modifying the distance between the T cell and cancer cells may lead to some unpredictability in the art. We note, however, that "a patent does not need to guarantee that the invention works for a claim to be enabled." *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1189 (Fed. Cir. 2014).

e) The quantity of experimentation necessary

Petitioner asserts that in light of the factors discussed above, a person of ordinary skill in the art would have had to "undertake an iterative, trial-and-error process . . . to practice the broad scope of the claims" and that such experimentation would have been "significant." Pet. 33–34 (citing Ex. 1002 ¶¶ 85–92).

Patent Owner responds, stating Petitioner fails to support its assertion that the amount of experimentation would be "significant." Prelim. Resp. 57. Patent Owner contends that Petitioner's conclusory assertion is contradicted by other portions of the Petition that admit that FDA-approved antibodies that target cancer cells were well known before 2020 (Pet. 49, 59–60); the 2010 Provisional describes fourteen tags that can be conjugated to antibodies (*id.* at 28); attaching the tags would have been "trivial" (*id.* at 59); CAR T cells were readily available before 2010 (*id.* at 9, 49, 59–65); and the level of ordinary skill in the art was high (*id.* at 33). Prelim. Resp. 58–59. According to Patent Owner, "[t]he only experiment to be done was to use the admittedly readily available materials as described in the 2010 Provisional." *Id.* at 59.

On this record, we find Patent Owner's argument persuasive. Petitioner has not sufficiently explained why the quantity of experimentation would have weighed in favor of undue experimentation. Petitioner merely asserts that it would have been "significant," but does not specify what that experimentation would have entailed, particularly in light of the high level of skill in the art and the known methods needed to practice the invention, as explained by Patent Owner. *See* Prelim. Resp. 58–59; *see also Wands*, 858 F.2d at 740 (finding no undue experimentation where "[t]here was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known").

f) Practical utility for the invention

According to the Federal Circuit, "the how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention." *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1323, 1324 (Fed.

Cir. 2005) (citation omitted). However, "[t]he bar for utility is not high." *Grunenthal GmBH v. Alkem Labs Ltd.*, 919 F.3d 1333, 1345 (Fed. Cir. 2019). "[A] patent has utility if the alleged invention is capable of providing some identifiable benefit presently available to the public." *Id.*

Petitioner argues the 2010 Provisional fails to disclose a practical utility for the invention because it does not contain in vitro or in vivo data to support the therapeutic effectiveness in treating cancer. Pet. 34. As support, Petitioner relies on *Rasmusson* and *In re '318 Patent Infringement Litigation*, 583 F.3d 1317 (Fed. Cir. 2009), and argues that "the '125 patent claims a 'therapeutically-effective' method of treatment that was unproven in the art . . . at the time of the 2010 Provisional." *Id.* at 35–36.

Patent Owner responds, noting the 2010 Provisional identifies the utility of the claims: "[t]he instant invention allows for the treatment of various diseases including cancer, inflammatory area, and other physiological and pathological sites." Prelim. Resp. 59–60 (quoting Ex. 1004, 2). Patent Owner also notes the 2010 Provisional states that the "universal ATCAR provides a more efficient process than current Chimeric-Antigen-Receptor approaches." *Id.* (quoting Ex. 1004, 2). Moreover, Patent Owner asserts Petitioner applies the wrong legal standard because experimental data is not always required to show utility. Prelim. Resp. 60 (citing *Grunenthal GmbH v. Alkem Labs Ltd.*, 919 F.3d 1333, 1346 (Fed. Cir. 2019) ("While test results often support claims of utility in patents concerning pharmacological arts, such testing is not always required.")). Patent Owner distinguishes the *Rasmusson* and *In re '318 Patent* cases and cites the four experiments disclosed in the '125 patent as demonstrating utility. *Id.* at 61 (citing Ex. 1001, 15:22–18:48).

As an initial matter, we reject Patent Owner's argument that the experiments disclosed in the '125 patent establish the utility of the claimed invention for purposes of priority. We are considering whether the 2010 Provisional enables the claims. Any disclosures of the '125 patent specification are inapposite.

That said, we are not persuaded that *Rasmusson* and *In re '318 Patent* apply to the facts and circumstances of this case. In *Rasmusson*, the claims were directed to a method of treating prostate cancer in humans with finasteride, which is a selective 5αR inhibitor. 413 F.3d at 1323. At the time of the earlier-filed applications, it was not known that 5αR inhibition contributed to any anti-tumor effects because the cause of prostate cancer was not known. *Id.* at 1324.

In *In re '318 Patent*, the claims were directed to a method of treating Alzheimer's disease with galanthamine. 583 F.3d at 1320. The specification described various animal tests, but the inventor and the patentee's witnesses testified that "the utility of the invention could not be inferred from the prior art testing described in the specification." *Id.* at 1325. Moreover, the inventor testified that when he submitted the patent application, he "certainly wasn't sure, and a lot of other people weren't sure that cholinesterase inhibitors[, a category of agents that includes galanthamine,] would ever work." *Id.* at 1327 (citation omitted).

Here, in contrast, the claims are directed to a method of treating cancer using techniques that were known to be useful in the art as of the filing date of the 2010 Provisional. *See, e.g.*, Ex. 1037 (2010 review article regarding the use of CAR-T cells for cancer immunotherapy); *see also* Ex. 1001, 1:43–50 (citing various pre-clinical and early-phase clinical trials from 2006 and 2008 using CAR T cells to treat cancer patients). Indeed,

Petitioner's expert noted that "multiple generations of CARs had been widely examined in the art." Ex. 1002 ¶ 62 (citing Ex. 1037). Thus, on this record, we find the 2010 Provisional discloses practical utility for the claimed invention, as we are not persuaded that the case law cited by Petitioner requires the 2010 Provisional to disclose experimental data to demonstrate utility, as Petitioner asserts.

g) Conclusion as to enablement

Having considered the parties' arguments regarding the various *Wands* factors and the utility of the claimed invention, we find on balance that Petitioner has not established a reasonable likelihood of showing a person of ordinary skill in the art would not have been able to practice the claimed invention without undue experimentation.

4. Whether Patent Owner Conceded the Later Effective Filing Date

Finally, Petitioner argues that Patent Owner effectively conceded the priority date for the '125 patent is 2011 and not 2010 during prosecution of the continuation application. Pet. 36. Specifically, Petitioner notes that in the declaration submitted by Patent Owner, Dr. Kaiser states that he is "familiar with the knowledge of one skilled in the art . . . as of ***the December 14, 2011 effective filing date*** of the above-referenced U.S. patent application." *Id.* at 37 (quoting Ex. 1005, 1) (emphasis added by Petitioner). Petitioner also notes that Patent Owner never challenged the examiner's statement that the 2010 Provisional "fails to provide adequate support or enablement" for the pending claims, which were similar to claims 2–21 of the '125 patent. *Id.* at 37–38 (quoting Ex. 1056, 18) (emphasis omitted). Because the '125 patent claims are comparable in scope to, or even broader than, the continuation application claims, Petitioner argues Patent Owner

implicitly conceded the effective filing date of the '125 patent is December 14, 2011. *Id.* at 38.

Patent Owner does not explicitly address Petitioner's argument regarding the alleged concession, but we are not persuaded by Petitioner's argument on its face. We consider Petitioner's argument to be akin to the doctrine of prosecution history disclaimer for claim construction. The Federal Circuit has repeatedly found that "an applicant's silence regarding statements made by the examiner during prosecution, without more, cannot amount to a 'clear and unmistakable disavowal' of claim scope." *Salazar v. Procter & Gamble Co.*, 414 F.3d 1342, 1344 (Fed. Cir. 2005); *see also 3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1373–74 (Fed. Cir. 2003) ("An applicant's silence in response to an examiner's characterization of a claim does not reflect the applicant's clear and unmistakable acquiescence to that characterization if the claim is eventually allowed on grounds unrelated to the examiner's unrebutted characterization."). During prosecution of the continuation application, there could have been several reasons why Patent Owner did not challenge the examiner's statement regarding the effective filing date. For example, Patent Owner may have believed it was easier to traverse the rejection on the merits, which would explain why its declarant applied December 14, 2011, as the effective filing date of the continuation application. Given there was no clear and unmistakable acquiescence by Patent Owner to the examiner's statement, we do not find persuasive Petitioner's argument that Patent Owner conceded the effective filing date of the '125 patent.

5. Conclusion

On this record, having considered the specific arguments raised in the Petition and Preliminary Response, we find Petitioner has not shown a

reasonable likelihood of establishing that the '125 patent claims are not entitled to the benefit of the filing date of the 2010 Provisional. For purposes of this proceeding, we therefore apply December 14, 2010, as the effective filing date of the '125 patent claims.

D. Unpatentability over UPenn and Ang

Each ground of unpatentability asserted in the Petition relies on one or both of UPenn and Ang. Pet. 25–26.

UPenn was filed on September 24, 2012, and claims priority to U.S. Provisional Application No. 61/537,933, which was filed on September 22, 2011. Ex. 1008, at [22], [30]. Even if UPenn were entitled to the benefit of the filing date of its provisional application, which Patent Owner contests (Prelim. Resp. 30–34), the earliest effective filing date of UPenn is September 22, 2011, which is after the December 14, 2010, effective filing date that we apply to the '125 patent claims in this proceeding.

Ang is an abstract printed in the journal *Molecular Therapy*. Ex. 1006. Petitioner alleges that Ang was published and publicly available on May 1, 2011. Pet. 17; Paper 12. Even if we were to find Ang is a printed publication, which Patent Owner contests (Prelim. Resp. 17–30; Paper 15), the earliest asserted publication date of Ang is May 1, 2011, which is after the December 14, 2010, effective filing date that we apply to the '125 patent claims in this proceeding.

Because we find neither UPenn nor Ang is prior art on this record, we determine Petitioner has not demonstrated a reasonable likelihood of prevailing on any ground in this proceeding.

E. Remaining Arguments

Patent Owner asserts that it, as an alter ego of the State of Maryland, is immune from this administrative proceeding under the doctrine of state

sovereign immunity. Prelim. Resp. 10–11. The Federal Circuit has ruled that states are not immune from *inter partes* review proceedings. *Regents of the Univ. of Minn. v. LSI Corp.*, 926 F.3d 1327 (Fed. Cir. 2019). Since Patent Owner filed its Preliminary Response, the Supreme Court denied the Petition for Writ of Certiorari. *Regents of the Univ. of Minn. v. LSI Corp.*, 140 S. Ct. 908 (Mem.) (2020). Accordingly, the Federal Circuit's decision stands and we reject Patent Owner's state sovereign immunity argument.

Patent Owner also argues that the Petition should be denied because it utilized improper spacing techniques and improperly incorporated by reference its expert's declaration testimony. Prelim. Resp. 12–14, 54–55. Because we find in favor of Patent Owner in rendering this Decision, we consider Patent Owner's arguments to be moot.[6]

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has not established a reasonable likelihood of prevailing on its assertions that claims 1–21 of the '125 patent are unpatentable over the cited art.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* as to all challenged claims of the '125 patent and no trial is instituted.

[6] That said, we agree with Patent Owner that the spacing techniques in the Petition were improper. We advise Petitioner not to use such techniques in any future filings before the Board.

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