

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AJINOMOTO CO., INC.,
Petitioner,

v.

ABTIS CO., LTD.,
Patent Owner.

IPR2025-00283
Patent 11,896,675

Before JEFFREY N. FREDMAN, JO-ANNE M. KOKOSKI, and
LILAN REN, *Administrative Patent Judges*.

REN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Ajinomoto Co., Inc. (“Petitioner”) filed a Petition requesting *inter partes* review of claims 1–13 of U.S. Patent No. 11,896,675 (Ex. 1001, “the ’675 patent”). Paper 2 (“Pet.”). Petitioner filed a declaration of Dr. Lawrence Nathan Tumey (Ex. 1002) and a declaration of Dr. Tatsuy Okuzumi (Ex. 1003) in support of the Petition. AbTis Co., Ltd. (“Patent Owner”) filed a Preliminary Response. Paper 9 (“Prelim. Resp.”). Patent Owner also disclaimed claims 1–10, 12, and 13 of the ’675 patent, leaving only dependent claim 11 (“the challenged claim”) at issue in this proceeding. Ex. 2001 (disclaimer dated May 9, 2025); 37 C.F.R. § 42.107(e) (“No *inter partes* review will be instituted based on disclaimed claims.”).

We have authority to determine whether to institute an *inter partes* review. *See* 35 U.S.C. § 314 (2024); 37 C.F.R. § 42.4(a) (2024). Institution of an *inter partes* review requires that “the information presented in the petition . . . and any response . . . shows that 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). For the reasons set forth below, we determine that there is a reasonable likelihood that Petitioner will prevail with respect to claim 11 which is the sole remaining claim. We institute an *inter partes* review.¹

¹ The case was referred to the Board panel to consider the merits and non-discretionary considerations. Paper 13, 2.

II. BACKGROUND

A. Real Parties in Interest

Petitioner identifies itself as the real party in interest. Pet. 1. Patent Owner identifies itself as the real party in interest. Paper 3, 2 (Patent Owner Mandatory Notices).

B. Related Matters

Petitioner states they are “not aware of any other current litigation or administrative proceedings involving the ’675 Patent that would affect, or be affected by, a decision in this proceeding.” Pet. 1. Patent Owner does not contest this statement by the Petitioner. Paper 3, 2.

C. The ’675 Patent

The ’675 patent, titled “Site-Specific Antibody Conjugation and Antibody-Drug Conjugate as Specific Embodiment Therefore,” “relates to technology capable of labeling a certain site of an antibody with a certain number of chemical functional groups or cargo moieties.” Ex. 1001, codes (54), (57). The ’675 patent explains that “[a]ntibodies are biomolecules that have a function of recognizing certain molecules, and have been used for various industrial applications” and “for therapeutic purposes.” *Id.* at 1:35–41. “To expand the functions of such an antibody, there [have] been attempts to improve the antibody’s ability.” *Id.* at 1:43–44. For example, “when an antibody is labeled with an agent for treating a certain disease, the antibody may be used to maximize a therapeutic effect of the antibody. These attempts and technology are generally referred to as ‘antibody labeling.’” *Id.* at 1:48–53.

The ’675 patent seeks to address antibody labeling issues associated with “randomly attaching a foreign substance to an antibody.” *Id.* at 1:55–56. According to the ’675 patent, such random attachment “highly degraded

[an] antibody's ability to recognize by allowing a foreign substance to bind to an antigen-binding domain of an antibody or a site adjacent to the antigen-binding domain." *Id.* at 2:4–7.

The '675 patent thus "provides technology for specifically transferring a chemical functional group to lysine 246 in the antibody" allowing "uniformly labeling an antibody in a site-specific manner." *Id.* at 2:9, 2:26–28. More specifically, the '675 patent may provide technology both for "specifically transferring a chemical functional group" and "specifically linking a cargo moiety to lysine 248 in the antibody." *Id.* at 2:31–32, 2:51–52.

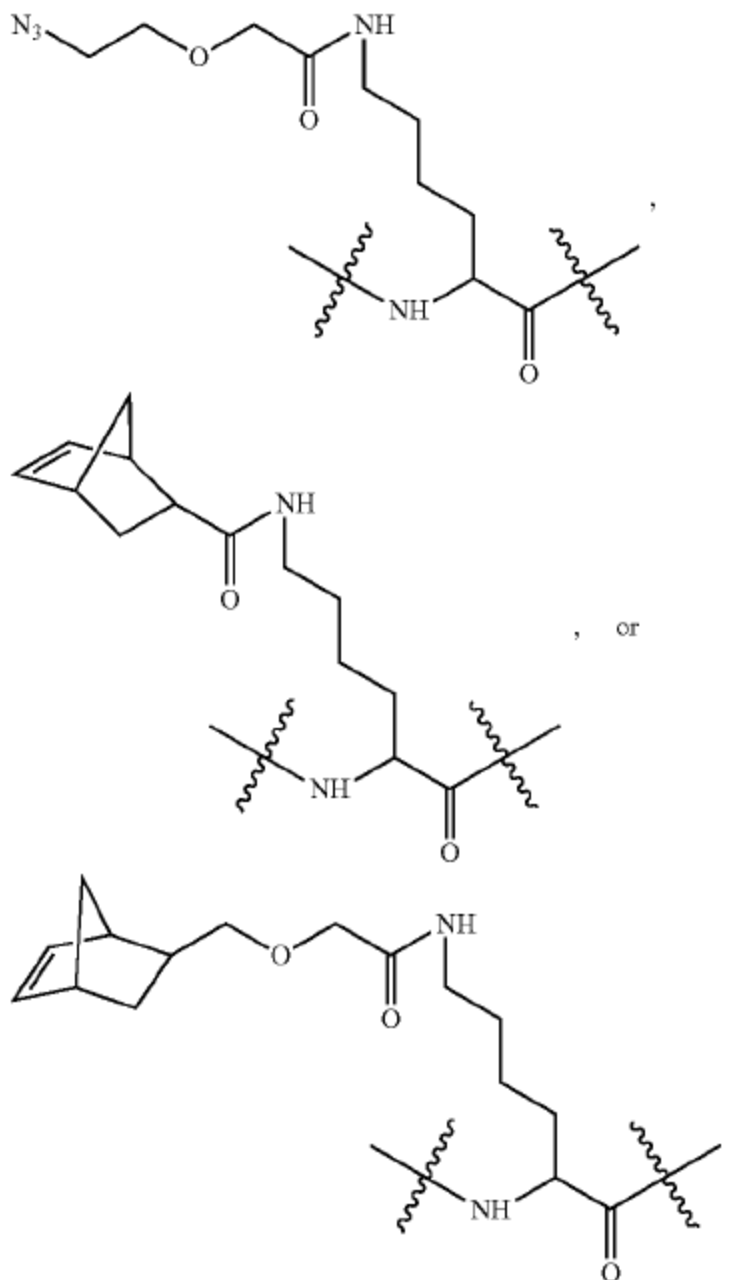
D. Illustrative Claim

Petitioner challenges claim 11 of the '675 patent, which depends from claim 1 (now statutorily disclaimed). Claim 1 and claim 11 are reproduced below with added bracketed reference numerals in which elements 1.pre through 1.d are recited in claim 1 and element 11.a is additionally recited in claim 11.

1. [1.pre] A modified antibody or its fragment comprising bio-orthogonal click chemistry functional group,
 - [1.a] wherein the modified antibody comprises one or more modified heavy chain,
 - [1.b] wherein each of the modified heavy chain comprises a modified lysine residue at 248 position of heavy chain amino acid sequence, wherein the 248 position is determined by an EU numbering system, and
 - [1.c] wherein the modified lysine residue comprises a bio-orthogonal click chemistry functional group at terminal end, and
 - [1.d] wherein the modified lysine residue does not comprise a terminal bio-reactive functional group selected from terminal hydroxy group, terminal carboxyl group,

terminal thiol group, terminal amino group, and terminal aldehyde group.

11. The modified antibody of claim 1,
[11.a] wherein the modified lysine residue has following structure:



Ex. 1001, 179:1–17, 180:11–48.

E. Asserted Grounds of Unpatentability

Petitioner asserts that the claim 11 would have been unpatentable on the following grounds:

Ground ²	Claim(s) Challenged	35 U.S.C. § ³	Reference(s)/Basis
1	11	102	CA959 ⁴
3	11	103	PepTalk Poster ⁵ , Yamada ⁶

² As a result of Patent Owner’s statutory disclaimer, only grounds 1, 3, 5, and 7 as applicable to the sole remaining claim 11 remain in this proceeding.

³ The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the filing date of the application for the ’675 patent was after that date, we refer to the post-AIA versions of §§ 102 and 103.

⁴ CA 3132959 A1 (“CA959”), published Sep. 17, 2020, filed Mar. 9, 2020 (Ex. 1005). CA959 claims priority to U.S. Provisional Application No. 62/815,557, filed on March 8, 2019. Petitioner contends that CA959 is prior art to the ’675 patent. Pet. 22.

⁵ PepTalk Poster, “Development of a Novel Chemical Site-Specific Conjugation Platform for ADCs.” According to Petitioner, this poster was presented at an annual scientific conference called “PepTalk: The Protein Science Week” held from January 14–18, 2019 (Ex. 1006). Pet. 23. Petitioner contends that PepTalk Poster is prior art to the ’675 patent. *Id.*

⁶ Yamada, WO 2020/199337, published June 18, 2020, filed Oct. 25, 2019, which claims priority to Japanese Patent Application No. 2017-090679, filed on April 28, 2017 (Exs. 1008, 1009 (US Application Pub. No. 2020/0190165)). Petitioner contends that Yamada is prior art to the ’675 patent under 35 U.S.C. § 102(a)(1). Pet. 28. Petitioner states that the English translation is certified. Ex. 1009, 1–2.

Ground ²	Claim(s) Challenged	35 U.S.C. § ³	Reference(s)/Basis
5	11	103	PepTalk Presentation ⁷ , Yamada
7a	11	103	Yamada
7b	11	103	Yamada, Matsuda ⁸

Pet. 2–3.⁹

III. ANALYSIS

A. Legal Standards

A claim may be unpatentable as anticipated if “each and every limitation is found either expressly or inherently in a single prior art reference.” *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1375 (Fed. Cir. 2006) (citation omitted). Anticipation under § 102 may be established

⁷ PepTalk Presentation. According to Petitioner, this presentation was presented at the same conference as PepTalk Poster (Ex. 1007). Pet. 26. Petitioner contends that PepTalk Presentation is prior art to the ’675 patent. *Id.*

⁸ Matsuda, US 2021/013954, published May 13, 2021, filed Dec. 11, 2020 which claims priority to Japanese Patent Application No. 2018-113962, filed Jun. 14, 2018 (Exs. 1010, 1011 (English translation)). Petitioner contends that Matsuda is prior art to the ’675 patent under 35 U.S.C. § 102(a)(2). Pet. 28. Petitioner states that the English translation is certified. Ex. 1011.

⁹ Subsequent to the filing of Patent Owner’s statutory disclaimer, Petitioner clarifies that, in challenging the patentability of claim 11, “Ground 3 relies on PepTalk Poster and Yamada,” “Ground 5 relies on PepTalk Presentation and Yamada,” whereas “Ground 7 cites Matsuda with respect to certain elements of Claim 1. [sic] from which Claim 11 depends, but only in the alternative to obviousness based on Yamada alone.” Paper 12, 4; *cf.* Pet. 2–3 (stating that for challenged claims 1–11, Ground 3 is over PepTalk Poster alone or in combination with Yamada and Matsuda, Ground 5 is over PepTalk Presentation alone or in combination with Yamada and Matsuda, and Ground 7 is over Yamada in view of Matsuda).

by showing, as a matter of fact, that all elements arranged as specified in a claim are disclosed within the four corners of a reference, either expressly or inherently, in a manner enabling one skilled in the art to practice an embodiment of the claimed invention without undue experimentation. *See ClearValue, Inc. v. Pearl River Polymers, Inc.*, 668 F.3d 1340, 1344 (Fed. Cir. 2012).

A patent claim is unpatentable under 35 U.S.C. § 103 if “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” The question of obviousness is resolved based on underlying factual determinations, including (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) when presented, objective evidence of obviousness or nonobviousness, i.e., secondary considerations.¹⁰ *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

The obviousness inquiry typically requires an analysis of “whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (requiring “articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”)). A patent claim “is not proved obvious merely by demonstrating that each of its elements was, independently, known in the

¹⁰ Neither party presents evidence or arguments regarding objective evidence of non-obviousness. *See* Pet.; Prelim. Resp.

prior art.” *Id.* In particular, “[a]lthough the *KSR* test is flexible, the Board ‘must still be careful not to allow hindsight reconstruction of references . . . without any explanation as to *how* or *why* the references would be combined to produce the claimed invention.’” *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1066 (Fed. Cir. 2016) (alteration in original) (quoting *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1368 (Fed. Cir. 2012) (emphases added)). An obviousness determination based on a combination of references requires finding “both ‘that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.’” *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367–68 (Fed. Cir. 2016) (quoting *Kinetic Concepts*, 688 F.3d at 1360); *see KSR*, 550 U.S. at 418. Petitioner cannot satisfy its burden of proving obviousness by employing “mere conclusory statements,” but “must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.” *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016); *see also In re NuVasive, Inc.*, 842 F.3d 1376, 1383 (Fed. Cir. 2016) (a finding of a motivation to combine “must be supported by a ‘reasoned explanation’” (citation omitted)).

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3)); *see also Intelligent Bio-Sys.*, 821 F.3d at 1369. Therefore, to prevail in an *inter partes* review, Petitioner must explain how the prior art or the proposed combinations of prior art would have rendered the challenged claims unpatentable. At this preliminary

stage, we determine whether the information presented in the Petition shows there is a reasonable likelihood that Petitioner would prevail in establishing that claim 11 would have been anticipated by the prior art and/or rendered obvious over the proposed combinations of prior art. *See* 35 U.S.C. § 314(a).

B. Level of Ordinary Skill in the Art

Determining whether an invention would have been obvious under 35 U.S.C. § 103 requires resolving the level of ordinary skill in the pertinent art at the time the invention was made. *Graham*, 383 U.S. at 17. The person of ordinary skill in the art is a hypothetical person who knows the relevant art. *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995). Factors in determining the level of ordinary skill in the art include the types of problems encountered in the art, the sophistication of the technology, and the educational level of active workers in the field. *Id.* One or more factors may predominate. *Id.*

Petitioner contends that a person of ordinary skill in the art (“POSA”) in the field of the ’675 patent

as of the earliest claimed priority date or the filing date of the ’675 Patent would have had specialized knowledge in the field of antibody-drug conjugates, which would entail (1) a Ph.D. degree in organic chemistry, biochemistry, medicinal chemistry, and/or pharmacology, along with at least 1-2 years of relevant applied research and/or industry experience in the field of antibodies or antibody-drug conjugates, or, alternatively, (2) a Master’s or Bachelor’s degree in one of the aforementioned fields with at least 3-5 years, or 5-7 years, respectively, of relevant applied research and/or industry experience in the field of antibodies or antibody-drug conjugates. That person would have familiarity, gained through study, training, and/or experience, with the design and development of antibody-drug conjugates and antibody modifications.

Pet. 3 (citing Ex. 1002 ¶ 36).

Patent Owner does not address this issue at this stage of the proceeding. *See generally* Prelim. Resp.

For purposes of this Decision, we adopt Petitioner’s unopposed definition of the level of ordinary skill in the art as it appears consistent with the disclosures of the ’675 patent and the prior art of record. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

C. Claim Construction

In an *inter partes* review, we apply the same claim construction standard as would be used by a district court to construe a claim in a civil action involving the validity or infringement of a patent. 37 C.F.R. § 42.100(b). Under that standard, claim terms are given their ordinary and customary meaning, as would have been understood by a person of ordinary skill in the art at the time of the invention, in light of the language of the claims, the specification, and the prosecution history of record. *Id.*; *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc); *Thorner v. Sony Comput. Entm’t Am. LLC*, 669 F.3d 1362, 1365–66 (Fed. Cir. 2012). “The Board is required to construe ‘only those terms . . . that are in controversy, and only to the extent necessary to resolve the controversy.’” *Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375 (Fed. Cir. 2019) (quoting *Vivid Techs., Inc. v. Am. Sci. Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

Petitioner proposes express construction for multiple claim terms. Pet. 9–13. At this stage of the proceeding, Patent Owner does not address Petitioner’s proposed claim construction, nor does Patent Owner propose its own claim construction. *See generally* Prelim. Resp. After reviewing Petitioner’s arguments and the evidence currently before us, we determine

that we do not need to expressly construe any claim term to resolve any controversy at this stage of the proceeding.

D. Earliest Effective Filing Date

The '675 patent, filed on January 16, 2023, is a continuation of U.S. Application No. 16/980,503, filed on September 14, 2020, which claims priority to the March 8, 2019 filing of provisional application 62/815,557 (“provisional application”). Ex. 1001, codes (63), (60). Patent Owner argues that the '675 patent is entitled to the March 8, 2019 priority date. Prelim. Resp. 4–5.

Petitioner, on the other hand, argues that the '675 patent is only entitled to the later priority date of January 16, 2023, which is the filing date of the application that issued as the '675 patent. Pet. 13–22. Petitioner argues that claim element 1.d (which recites certain negative limitation excluding terminal aldehyde groups and other terminal functional groups) lacks written description support in the provisional application and is therefore not entitled to the benefit of the earlier March 8, 2019 priority date. *Id.* Petitioner argues that “the applications underlying the '675 Patent are entirely silent regarding terminal aldehyde groups” and such groups “are never disclosed or discussed in the context of a terminal bio-reactive functional group, nor is there any example using such a group.” *Id.* at 17 (citing Ex. 1002 ¶¶ 76, 77; Ex. 1037; Ex. 1040). Petitioner argues that claims 2–13 lack written description support based on their dependency from claim 1 and therefore are not entitled to the priority date of March 8, 2019, and specifically argues that claims 2, 3, 5–7, 12, and 13 lack written description support. *Id.* at 18, 19–22.

Patent Owner argues that claim 11, notwithstanding its dependency from claim 1, is sufficiently supported by the provisional application

because “[n]one of the three structures recited in Claim 11 comprise a ‘terminal bio-reactive functional group selected from terminal hydroxy group, terminal carboxyl group, terminal thiol group, terminal amino group, and terminal aldehyde group’ as recited by disclaimed Claim 1.” Prelim. Resp. 10. Therefore, Patent Owner argues, “the inclusion of the three specific modified lysine terminal groups necessarily excludes the terminal groups contained in the negative limitation, and is sufficiently supported in the specification of the ’675 Patent.” *Id.* at 10–11 (footnote omitted). Patent Owner also argues that because claim 1 has been disclaimed, the negative limitation of claim element 1.d “is no longer applicable” and “is effectively negated by the addition of the specific structure in Claim 11.” *Id.* at 9.

“It is elementary patent law that a patent application is entitled to the benefit of the filing date of an earlier filed application only if the disclosure of the earlier application provides support for the claims of the later application, as required by 35 U.S.C. § 112.” *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1306 (Fed. Cir. 2008) (citations omitted); *see also Research Corps. Techs. v. Microsoft Corp.*, 627 F.3d 859, 871–72 (Fed. Cir. 2010) (holding that claims of the later-filed application, which were not limited to a “blue noise mask,” were “not entitled to claim the benefit of their parent applications’ filing dates”); *ICU Med., Inc. v. Alaris Med. Sys.*, 558 F.3d 1368, 1377–78 (Fed. Cir. 2009) (holding that “spikeless” claims “added years later during prosecution” were not supported by the specification which “describe[d] only medical valves with spikes”); *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1158–60 (Fed. Cir. 1998) (holding the generic shaped cup claims of the later-filed child application were not entitled to the filing date of the parent application that “disclosed only a trapezoidal cup and nothing more”). “To satisfy the written description

requirement the disclosure of the prior application must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, [the inventor] was in possession of the invention.” *PowerOasis*, 522 F.3d at 1306 (emphasis omitted; alteration in original; citations and quotations omitted). The sufficiency of written description support is based on “an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.” *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). “Negative claim limitations are adequately supported when the specification describes a reason to exclude the relevant limitation.” *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1351 (Fed. Cir. 2012).

“In an *inter partes* review, the burden of persuasion is on the petitioner to prove ‘unpatentability by a preponderance of the evidence,’ . . . and that burden never shifts to the patentee.” *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (quoting 35 U.S.C. § 316(e)). The burden of production can shift to the patentee, however (*see id.* at 1379), where it is “warranted because the patentee affirmatively seeks to establish a proposition not relied on by the patent challenger and not a necessary predicate for the unpatentability claim asserted—effectively an affirmative defense.” *In re Magnum Oil*, 829 F.3d at 1376.

In this case, claim 11, as it is currently written, depends from claim 1 and therefore requires that all of the limitations of claim 1, including the negative limitation of claim element 1.d, have written description support in

the provisional application.¹¹ The terminal functional groups excluded as the negative limitation must be supported through an “express disclaimer or independent lexicography in the written description.” *Omega Eng’g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323 (Fed. Cir. 2003). The parties agree that “the applications underlying the ’675 Patent are entirely silent regarding terminal aldehyde groups.” Pet. 17; *see* Prelim Resp. 9–10. Patent Owner’s argument that these underlying applications reasonably convey possession to a POSA does not cite to evidence in the record as support. *See* Prelim Resp. 9. Patent Owner argues that the specific structures recited in claim element 11.a “necessarily exclude[] the terminal groups contained in the negative limitation” (*id.* at 9–10) but does not sufficiently explain why there is the requisite “express disclaimer or independent lexicography” (*Omega Eng’g*, 334 F.3d at 1323) to exclude only these particular terminal functional groups but not others. Although the scope of claim 11 is limited to those structures specifically recited, the record before us does not sufficiently show why the inclusion of these structures in element 11.a excludes only the particular terminal functional groups in the negative limitation but not others.

We preliminarily determine, based on the record before us, that Petitioner has adequately established that the provisional application does not provide written description support for claim 11 as it is currently written. Accordingly, at this stage of the proceeding, Petitioner has sufficiently

¹¹ We note that Patent Owner represents that, “[t]o the extent the Board is inclined to hold that current Claim 11 is not adequately supported by the specification due to the negative limitation recited in disclaimed Claim 1, Patent Owner intends to amend Claim 11 into independent form and remove the reference to the negative limitation.” Prelim. Resp. 11 n.4.

shown that the earliest possible filing date of the '675 patent is January 16, 2023, which is the filing date of the application that issued as the '675 patent, for purposes of institution.

E. Alleged Anticipation Over CA959 (Ground 1)

Petitioner alleges claim 11 of the '675 patent is anticipated by CA959, the disclosure of which is “essentially identical” to the '675 patent, because CA959 has a priority date of March 8, 2019 and is therefore prior art to the '675 patent. Pet. 13–19, 29–34, 37. Patent Owner responds that the '675 patent is entitled to the same priority date as CA959 and therefore CA959 “is not prior art, but is in fact in the priority chain for the '675 [p]atent.” Prelim. Resp. 8–9.

1. CA959

The parties agree that CA959 is entitled to the same priority date as the provisional application, filed on March 8, 2019. Pet. 22; Prelim. Resp. 5. The parties agree that CA959 and '675 patent contain essentially identical disclosures. Pet. 16; *see* Prelim. Resp. 9.

2. Analysis of Ground 1

At this stage of the proceeding, Patent Owner does not address Petitioner’s specific contentions with respect to the limitations of claim 11 (Pet. 31–34, 37). *See generally* Prelim. Resp. Based on our determination *supra* that claim 11 of the '675 patent is entitled to the January 16, 2023 priority date and based on our review and consideration of the current record with regard to the alleged anticipation by CA959, we determine that Petitioner has sufficiently shown that CA959 discloses all elements of claim 11 for purposes of institution. *See* Pet. 31–34, 37 (and evidence cited therein).

3. Conclusion Regarding Ground 1

Based on the reasons provided *supra*, we determine that the information presented in the Petition demonstrates a reasonable likelihood of showing that claim 11 is anticipated under 35 U.S.C. § 102 by CA959.

F. Alleged Obviousness Over PepTalk Poster & Yamada (Ground 3)

Petitioner alleges claim 11 of the '675 patent would have been obvious over PepTalk Poster and Yamada. Pet. 41–43, 45, 49–55. Patent Owner responds that Petitioner fails to establish a motivation to combine the references, or a reasonable expectation of success. Prelim. Resp. 11–18. Having considered the arguments and evidence before us, we find, for the reasons explained below, that the record establishes a reasonable likelihood that Petitioner would prevail in its challenge to claim 11 on this asserted ground of unpatentability.

1. PepTalk Poster¹²

Petitioner states that PepTalk Poster “was presented at an annual scientific conference called ‘PepTalk: The Protein Science Week’ held from January 14-18, 2019, in San Diego, California.” Pet. 23. PepTalk Poster relates to “antibody-drug conjugates (ADCs)” which “can be expected to provide treatment breakthroughs by offering increased efficacy and decreased toxicity compared to traditional chemotherapeutic cancer treatments.” Ex. 1006. PepTalk Poster describes a “site-specific conjugation

¹² Based on our review of the record before us, PepTalk Poster qualifies as prior art at this stage of the proceeding. *See* Pet. 23–26. Patent Owner does not contest the prior art status of this reference at this stage of the proceeding. *See generally* Prelim. Resp.

technique[]” known as AJICAP¹³ which may “conjugate payloads with a native mAbs [monoclonal antibody] chemically in a site-specific manner.” *Id.* Figure 1 below reproduces an illustration from PepTalk Poster showing the capability of the AJICAP technique. *Id.*

1. Capability of AJICAP™

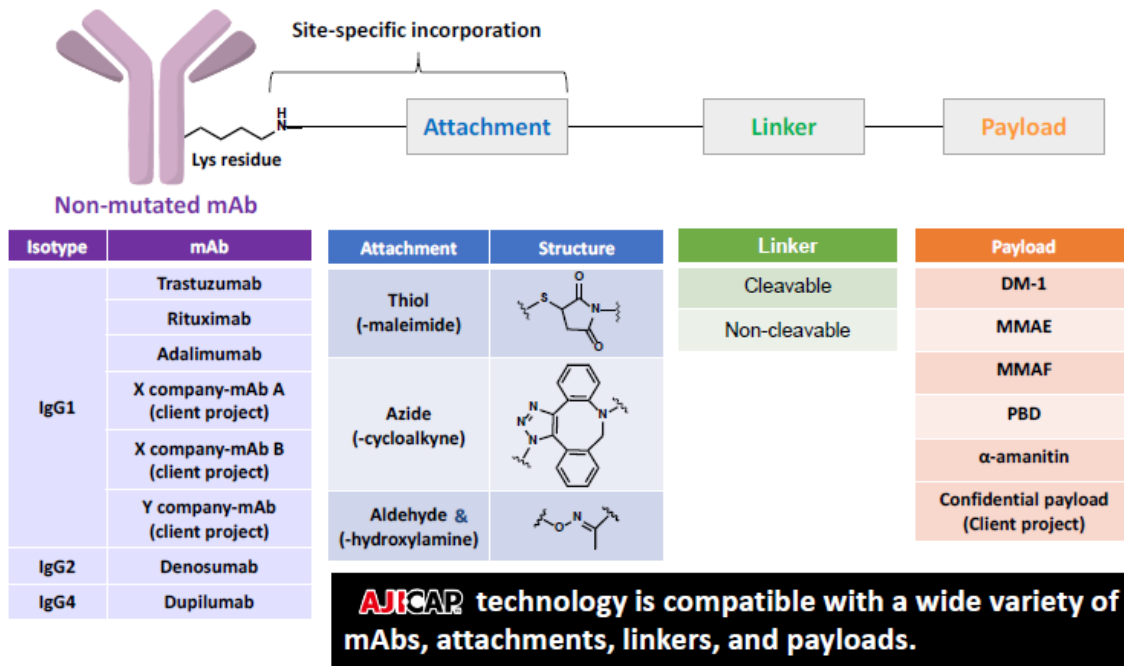


Fig. 1 - A reproduction of an illustration of PepTalk Poster

Figure 2 below reproduces an illustration from PepTalk Poster showing a target lysine residue as 248. *Id.*

¹³ The term “AJICAP” usually appears in the record with a trademark or “™” designation. *See, e.g.*, Ex. 1006. In this proceeding, we do not express any view on whether the term “AJICAP” is properly designated as a trademark.

2. Determine Target Lysine Residue

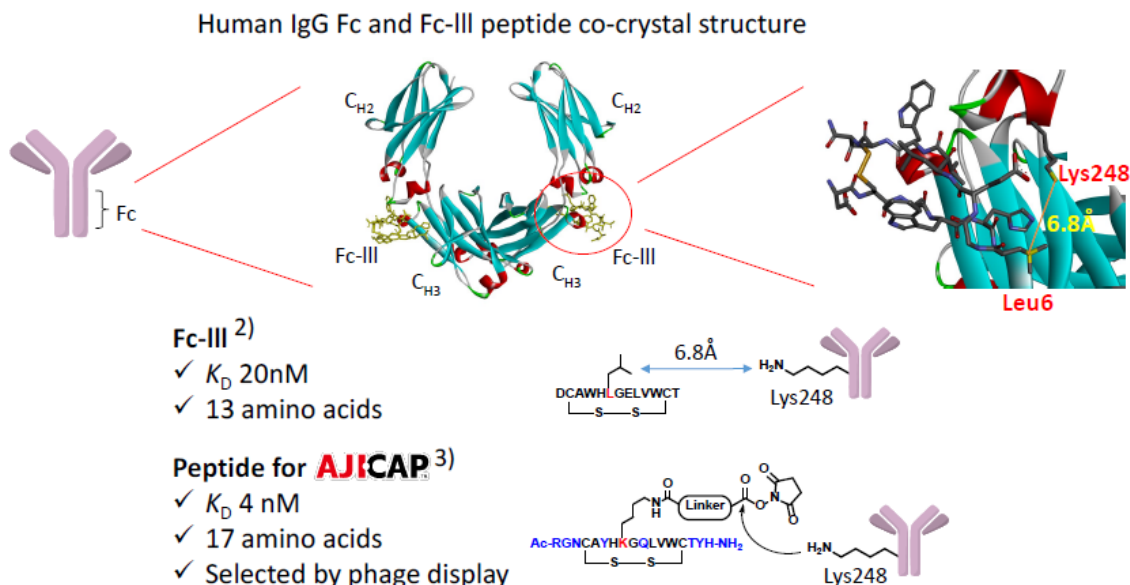


Fig. 2 - A reproduction of an illustration of PepTalk Poster

2. Yamada

Yamada, titled “Compound Having Affinity Substance to Soluble Protein, Cleavable Portion and Reactive Group, or Salt Thereof” “provides a technique enabling modification of a soluble protein and in particular regioselective modification of a soluble protein.” Ex. 1009, codes (54), (57). The ’675 patent describes Yamada in multiple paragraphs. Pet. 7. For example, the ’675 patent notes that Yamada “is similar to the present invention in terms of the form of an agent for transferring a first chemical functional group to an antibody, but is different . . . in that the cross-linker includes two NHS esters.” Ex. 1001, 33:4–8. The ’675 patent notes that Yamada “aims to site-selectively modulate lysine 246 or 248 in an Fc domain using an analogue of Fc-III and use a biorthogonal functional group.” *Id.* at 69:48–51. The ’675 patent, however, also states that “any lysine residue is highly likely to be labeled” in Yamada because “the first carbonyl group has high reactivity and has no vicinity condition for

reaction.” *Id.* at 69:54–56. According to the ’675 patent, this is because Yamada “uses a disuccinimidyl cross-linker” resulting in “the first carbonyl group and the second carbonyl group [being] equally highly reactive.” *Id.* at 69:51–53. The ’675 patent provides two reasons why “the uniformity and yield of the antibody may be inevitably low” when Yamada “site-selectively modulate[s] lysine 246 or 248 in an Fc domain using an analogue of Fc-III.” *Id.* at 70:13–18.

3. Reasons to Combine & Reasonable Expectation of Success

Petitioner argues that Yamada teaches the structures (claim element 11.a) recited in claim 11. Pet. 50. More specifically, Petitioner argues “there are two ways in which Formula (IV) [of Yamada] can be completed to arrive at the first and third structures of claim 11.” *Id.* at 52; *see also* Ex. 1002 ¶ 277 (stating that “the first and third structures recites in claim 11 of the ’675 Patent are disclosed in Yamada and could be predictably constructed based on Yamada’s disclosure”). Petitioner cites testimony from Dr. Lawrence Nathan Tumey as support for the position that “a POSA would combine [the structures in Yamada and PepTalk Poster] with a reasonable expectation of success.” *Id.* at 56 (citing Ex. 1002 ¶¶ 277, 280). Dr. Tumey states that combining the prior art references would be “based on simple substitutions.” Ex. 1002 ¶ 280.

Patent Owner argues that Petitioner fails to provide a motivation or a reason as to why a skilled artisan would have combined the references because “Petitioner mentions some iteration of ‘motivation’ only five times” and “only eight times” in the testimony by Dr. Tumey. Prelim. Resp. 12 (citing Pet. 4, 77, 78, 79; Ex. 1002 ¶¶ 60, 61, 62, 403, 421, 422). Patent Owner argues that Petitioner’s proposed combination is solely based on impermissible hindsight. *Id.* at 14. Patent Owner argues that Dr. Tumey’s

“near-verbatim recitation of the Petition” is neither persuasive nor helpful. *Id.* at 13. Patent Owner argues that Petitioner’s “conclusory assertion does not explain why a POSA would have had a reasonable expectation of success, nor does it address any technical challenges or compatibility concerns associated with the proposed combination.” *Id.* at 17.

Patent Owner does not cite any authority stating that in a proper obviousness analysis under 35 U.S.C. § 103, there is a bright line test for the frequency at which the phrase “motivation to combine” (or similar phrases) is repeated in the petition and/or testimony. Patent Owner’s argument regarding the purportedly low frequency in which Petitioner and/or Dr. Tumey uses such phrases (*see* Prelim. Resp. 12) does not rebut Petitioner’s testimonial and other evidence in support of Petitioner’s arguments regarding motivation.

For example, Dr. Tumey testifies that as of 2019, “there was an expectation that site-specific conjugation would decrease off-target toxicity and improve the pharmacokinetic properties of the ADC, and thus there was a clear motivation in the art to pursue technologies that allowed site-specific conjugation.” Ex. 1002 ¶ 60. Dr. Tumey cites as support Exhibit 1027, which is an article titled “Antibody-Drug Conjugate-Based Therapeutics: State of the Science” in the Journal of the National Cancer Institute. Ex. 1002 ¶ 60 (citing Ex. 1027, pg. 538); Ex. 1027.

Dr. Tumey also testifies that “those working in the field of ADCs were motivated to devise means for selectively modifying antibodies at particular sites in order to preserve the antibody’s functions and to achieve more consistent DAR values” and that “it was firmly established before March 2019 that the conjugation site on the antibody component, a well-defined DAR, and homogeneity of the ADC product were important

parameters that need to be considered in ADC development, and individuals of ordinary skill in the art had every incentive to develop methodologies that would allow for more predictable and defined ADC production.” Ex. 1002 ¶ 63. Dr. Tumey cites as support Exhibit 1028, which is an article titled “Current Status: Site-Specific Antibody Drug Conjugates” for the Journal of Clinical Immunology, as well as Exhibit 1029, which is an article titled “Antibody-Drug Conjugates: Possibilities and Challenges” for the Avicenna Journal of Medical Biotechnology. Ex. 1002 ¶ 63 (citing Ex. 1028, S101–S105; Ex. 1029, 1, 13–14); Ex. 1028; Ex. 1029.

Dr. Tumey testifies that combining PepTalk Poster and Yamada is “based on simple substitutions” and would have been predictable. Ex. 1002 ¶¶ 277, 280. Dr. Tumey further testifies that “PepTalk Poster discloses a modified antibody with lysine residues 248 modified with an azide group, and Yamada likewise discloses antibodies modified at lysine 248 . . . with an azide . . . or a norbornene.” *Id.* ¶ 271 (citing various portions of Ex. 1009). Dr. Tumey provides a flow diagram showing how “a POSA could envisage that the first and third structures recited in claim 11 by selecting the components of Formula (IV)” in Yamada. Ex. 1002 ¶¶ 276–277 (citing Formula IV in Ex. 1009); *see also* Ex. 1002 ¶¶ 272–275 (citing various portions of Ex. 1009, including teachings regarding Formula (IV)); Pet. 49–55. On this record, we credit Dr. Tumey’s testimony regarding a POSA’s motivation to combine PepTalk Poster and Yamada with a reasonable expectation of success.

Based on our review and consideration of the current record, we are persuaded that Petitioner has adequately shown for purposes of institution that there is sufficient rationale to combine as well as a reasonable

expectation of success in combining the teachings of PepTalk Poster and Yamada in the manner suggested.

4. Analysis of Ground 3

Petitioner argues that the combined teaching of PepTalk Poster and Yamada teaches all elements of claim 11. Pet. 42–43, 49–56.

At this stage of the proceeding, does not address Petitioner’s specific contentions with respect to the limitations of claim 11. *See generally* Prelim. Resp. Based on our review and consideration of the current record, we determine that Petitioner has sufficiently shown that the combination teaches all elements of claim 11 for purposes of institution. *See* Pet. 42–43, 49–56 (and evidence cited therein).

5. Conclusion Regarding Ground 3

Based on the reasons provided *supra*, we determine that the information presented in the Petition demonstrates a reasonable likelihood that Petitioner will prevail as to its contention that claim 11 would have been unpatentable under 35 U.S.C. § 103 in view of PepTalk Poster and Yamada.

*G. Alleged Obviousness Over PepTalk Presentation & Yamada
(Ground 5)*

Petitioner alleges claim 11 of the ’675 patent would have been obvious over PepTalk Presentation and Yamada. Pet. 57–60, 62, 65–68. Patent Owner responds that the Petitioner fails to establish a motivation to combine the references, or a reasonable expectation of success. Prelim. Resp. 11–18. Having considered the arguments and evidence before us, we find, for the reasons explained below, that the record establishes a reasonable likelihood that Petitioner would prevail on its arguments regarding claim 11 on this asserted ground of unpatentability.

*1. PepTalk Presentation*¹⁴

Petitioner states that PepTalk Presentation “was presented on January 16, 2019, at the same 2019 PepTalk conference” as PepTalk Poster. Pet. 26. According to Petitioner, the “PepTalk Presentation contains much of the same information as PepTalk Poster” with additional technical details. *Id.* at 57 (citing various portions of Ex. 1007).

2. Reasons to Combine & Reasonable Expectation of Success

Petitioner argues that Yamada teaches the structures (claim element 11.a) recited in claim 11. Pet. 65. More specifically, Petitioner argues “[a] POSA would need only make selections of disclosed substituents for Formula (IV) as shown in the flow charts below to arrive at the first and third structures of claim 11.” *Id.* at 66–68; *see also* Ex. 1002 ¶ 370 (stating that “there are two ways in which Formula (IV) can be completed to arrive at the first and third structures of claim 11”). Petitioner cites testimony from Dr. Tumey to support the contention that “a POSA would combine [the structures in Yamada and PepTalk Presentation] with a reasonable expectation of success.” *Id.* at 68 (citing Ex. 1002 ¶¶ 372, 375). Dr. Tumey states that combining PepTalk Presentation and Yamada would be “based on simple substitutions.” Ex. 1002 ¶ 375.

Patent Owner argues that Petitioner fails to provide a motivation or a reason as to why a skilled artisan would have combined the references because “Petitioner mentions some iteration of ‘motivation’ only five times” and “only eight times” in the testimony by Dr. Tumey. Prelim. Resp. 12

¹⁴ Based on our review of the record before us and for purposes of this Decision, PepTalk Poster qualifies as prior art. *See* Pet. 26–28. Patent Owner does not contest the prior art status of PepTalk Poster at this stage of the proceeding. *See generally* Prelim. Resp.

(citing Pet. 4, 77, 78, 79; Ex. 1002, ¶¶ 60, 61, 62, 403, 421, 422). Patent Owner argues that Petitioner’s proposed combination is solely based on impermissible hindsight. *Id.* at 14. Patent Owner argues that Dr. Tumey’s “near-verbatim recitation of the Petition” is neither persuasive nor helpful. *Id.* at 13. Patent Owner argues that Petitioner’s “conclusory assertion does not explain why a POSA would have had a reasonable expectation of success, nor does it address any technical challenges or compatibility concerns associated with the proposed combination.” *Id.* at 17.

As already noted, Patent Owner’s argument regarding the frequency of which Petitioner and/or Dr. Tumey uses phrases such as “motivation to combine” (*see* Prelim. Resp. 12) does not rebut Petitioner’s testimonial and other evidence in support of Petitioner’s arguments regarding motivation.

For example, Dr. Tumey testifies that as of 2019, “there was an expectation that site-specific conjugation would decrease off-target toxicity and improve the pharmacokinetic properties of the ADC, and thus there was a clear motivation in the art to pursue technologies that allowed site-specific conjugation.” Ex. 1002 ¶ 60 (citing Ex. 1027, 538).

Dr. Tumey also testifies that “those working in the field of ADCs were motivated to devise means for selectively modifying antibodies at particular sites in order to preserve the antibody’s functions and to achieve more consistent DAR values” and that “it was firmly established before March 2019 that the conjugation site on the antibody component, a well-defined DAR, and homogeneity of the ADC product were important parameters that need to be considered in ADC development, and individuals of ordinary skill in the art had every incentive to develop methodologies that would allow for more predictable and defined ADC production.” Ex. 1002 ¶ 63 (citing Ex. 1028, S101–S105; Ex. 1029, 1, 13–14).

Dr. Tumey testifies that combining PepTalk Presentation and Yamada is “based on simple substitutions” and would have been predictable. Ex. 1002 ¶ 375; *see also id.* ¶ 372. Dr. Tumey testifies that “PepTalk Presentation discloses a modified antibody with lysine residues 248 modified with an azide group, and Yamada likewise discloses antibodies modified at lysine 248 . . . with an azide . . . or a norbornene.” *Id.* ¶ 366 (citing various portions of Ex. 1007 and Ex. 1009). Dr. Tumey provides a flow diagram showing how “a POSA could envisage that the first and third structures recited in claim 11 by selecting the components of Formula (IV)” in Yamada. Ex. 1002 ¶¶ 371–372 (citing Formula IV in Ex. 1009); *see also* Ex. 1002 ¶¶ 367–370 (citing various portions of Ex. 1009 including teachings regarding Formula (IV)); Pet. 65–68. On this record, we credit Dr. Tumey’s testimony regarding a POSA’s motivation to combine PepTalk Presentation and Yamada with a reasonable expectation of success.

Based on our review and consideration of the current record, we are persuaded that Petitioner has sufficiently shown for purposes of institution that there is sufficient rationale to combine as well as a reasonable expectation of success in combining the teachings of PepTalk Presentation and Yamada in the manner suggested.

3. Analysis of Ground 5

Petitioner argues that the combined teaching of PepTalk Presentation and Yamada teaches all elements of claim 11. Pet. 58–60, 65–68. At this stage of the proceeding, Patent Owner does not address Petitioner’s specific contentions with respect to the limitations of claim 11. *See generally* Prelim. Resp. Based on our review and consideration of the current record, we determine that Petitioner has sufficiently shown that the combination teaches all elements of claim 11 for purposes of institution.

4. Conclusion Regarding Ground 5

Based on the reasons provided *supra*, we determine that the information presented in the Petition demonstrates a reasonable likelihood that Petitioner will prevail on its arguments that claim 11 is unpatentable under 35 U.S.C. § 103 in view of PepTalk Presentation and Yamada.

H. Alleged Obviousness Over Yamada (Ground 7a)

Petitioner alleges claim 11 of the '675 patent would have been obvious over Yamada. Pet. 69–76, 77, 80–83; Paper 12, 4. Patent Owner responds that Petitioner engages in hindsight reasoning and fails to establish a motivation to modify Yamada, or a reasonable expectation of success. Prelim. Resp. 11–18. Having considered the arguments and evidence before us, we find, for the reasons explained below, that the record establishes a reasonable likelihood that Petitioner would prevail with respect to its contentions regarding claim 11 on this asserted ground of unpatentability.

1. Reasons to Modify & Reasonable Expectation of Success

Petitioner asserts that, as shown in the obviousness analysis of grounds 3 and 5, *supra*, Formula (IV) of Yamada “can be constructed in a variety of ways that are encompassed by [claim] 11.” Pet. 73 (citing Ex. 1002 ¶¶ 266–280, 361–375). Petitioner argues that “Yamada provides motivation for a POSA to prepare an antibody regioselectively modified with a bio-orthogonal functional group at the lysine residue at position 248” and “explains prior ADC production methods result in nonuniformity and varying DARs.” According to Petitioner, because “[t]he DAR can impact a variety of pharmacokinetic parameters, . . . a POSA would be motivated to regioselectively modify an antibody to prepare consistent DARs.” *Id.* at 77 (citing Ex. 1005 ¶ 4, Ex. 1002 ¶ 421, Ex. 1027, 541). Petitioner argues that “[a] POSA would need only make selections of disclosed substituents for

Formula (IV) as shown in the flow charts below to arrive at the first and third structures of claim 11.” *Id.* at 81–83; *see also* Ex. 1002 ¶ 449 (stating that “there are two ways in which Formula (IV) can be completed to arrive at the first and third structures of claim 11”). Dr. Tumey states that “the first and third structures recite[d] in claim 11 of the ’675 Patent are disclosed in Yamada and could be predictably constructed based on Yamada’s disclosure.” Ex. 1002 ¶ 451.

Patent Owner argues that Petitioner fails to provide a motivation or a reason as to why a skilled artisan would have combined the references because “Petitioner mentions some iteration of ‘motivation’ only five times” and “only eight times” in the testimony by Dr. Tumey. Prelim. Resp. 12 (citing Pet. 4, 77, 78, 79; citing Ex. 1002 ¶¶ 60, 61, 62, 403, 421, 422). Patent Owner argues that Petitioner’s proposed modification is solely based on impermissible hindsight. *Id.* at 14. Patent Owner argues that Dr. Tumey’s “near-verbatim recitation of the Petition” is neither persuasive nor helpful. *Id.* at 13. Patent Owner argues that Petitioner’s “conclusory assertion does not explain why a POSA would have had a reasonable expectation of success, nor does it address any technical challenges or compatibility concerns associated with the proposed combination.” *Id.* at 17. Patent Owner further argues that “[t]he Petition is impermissibly ‘defining the problem’ *Yamada* address ‘in terms of [the] solution’ *Yamada* discloses, which constitutes improper hindsight reasoning.” *Id.* at 16 (alteration in original) (citing Pet. 77).

The current record shows that Petitioner cites a journal article (Ex. 1027) in addition to Yamada and Dr. Tumey’s testimony in support of the rationale to modify Yamada. Pet. 77 (citing Ex. 1005 ¶ 4; Ex. 1002 ¶ 421; Ex. 1027, 541). Patent Owner’s argument that Petitioner’s rationale is solely

based on Yamada's teachings which led to the purported impermissible hindsight is therefore unsupported by the record before us.

As discussed previously, Patent Owner's argument regarding the purported frequency of which Petitioner and/or Dr. Tumey uses phrases such as "motivation to combine" (*see* Prelim. Resp. 12) does not rebut Petitioner's testimonial and other evidence in support of Petitioner's argument regarding motivation.

For example, Dr. Tumey testifies that as of 2019, "there was an expectation that site-specific conjugation would decrease off-target toxicity and improve the pharmacokinetic properties of the ADC, and thus there was a clear motivation in the art to pursue technologies that allowed site-specific conjugation." Ex. 1002 ¶ 60 (citing Ex. 1027, 538); Ex. 1027.

Dr. Tumey also testifies that "those working in the field of ADCs were motivated to devise means for selectively modifying antibodies at particular sites in order to preserve the antibody's functions and to achieve more consistent DAR values" and that

it was firmly established before March 2019 that the conjugation site on the antibody component, a well-defined DAR, and homogeneity of the ADC product were important parameters that need to be considered in ADC development, and individuals of ordinary skill in the art had every incentive to develop methodologies that would allow for more predictable and defined ADC production.

Ex. 1002 ¶ 63 (citing Ex. 1028, S101-S105; Ex. 1029, 1, 13–14); Ex. 1028; Ex. 1029.

Dr. Tumey testifies that Yamada "provides motivation for those skilled in the art to prepare an antibody regioselectively modified with a bio-orthogonal functional group at the lysine residue at position 248." Ex. 1002

¶ 403. Dr. Tumey testifies that “Yamada discloses an antibody modified at lysine residue 248 to include a bio-orthogonal click chemistry function group, including a terminal azide group.” *Id.* ¶ 424. Dr. Tumey testifies that “[t]he DAR of an ADC can influence its stability, solubility, antigen binding, clearance and biodistribution, resulting in different DAR species having distinct pharmacokinetics behaviors.” *Id.* ¶ 421 (citing various portions of Ex. 1005 and Ex. 1027). Based on these prior art teachings, Dr. Tumey concludes that “a person of ordinary skill would be motivated to regioselectively modify an antibody in order to prepare ADCs with a known and consistent DAR so that the pharmacokinetic properties of the ADC can be consistent.” Ex. 1002 ¶ 421; *see also id.* ¶ 403. Dr. Tumey provides a flow diagram showing how “a POSA could envisage that the first and third structures recited in claim 11 by selecting the components of Formula (IV)” in Yamada. Ex. 1002 ¶¶ 450–451 (citing Formula IV in Ex. 1009); *see also* Ex. 1002 ¶¶ 445–449 (citing various portions of Ex. 1009 including teachings regarding Formula (IV)); Pet. 80–83. We credit Dr. Tumey’s testimony regarding a POSA’s motivation to modify Yamada with a reasonable expectation of success.

Based on our review and consideration of the current record, we are persuaded that Petitioner has adequately shown for purposes of institution that there is sufficient rationale to modify Yamada in the manner suggested.

2. Analysis of Ground 7a

Petitioner argues that the Yamada teaches or suggests all elements of claim 11. Pet. 69–76, 77, 80–83.

At this stage of the proceeding, Patent Owner does not address Petitioner’s specific contentions with respect to the limitations of claim 11. *See generally* Prelim. Resp. Based on our review and consideration of the

current record, we determine that Petitioner has sufficiently shown that Yamada teaches or suggests all elements of claim 11 for purposes of institution.

3. Conclusion Regarding Ground 7a

Based on the reasons provided *supra*, we determine that the information presented in the Petition demonstrates a reasonable likelihood that Petitioner will prevail on its assertions that claim 11 would have been unpatentable under 35 U.S.C. § 103 in view Yamada.

I. Alleged Obviousness Over Yamada & Matsuda (Ground 7b)

Petitioner alleges claim 11 of the '675 patent would have been obvious over Yamada and Matsuda. Pet. 77–79, 80–83; Paper 12, 4. Patent Owner responds that the Petitioner engages in hindsight reasoning and fails to establish a motivation to combine the references, or a reasonable expectation of success. Prelim. Resp. 11–18. Having considered the arguments and evidence before us, we find, for the reasons explained below, that the record establishes a reasonable likelihood that Petitioner would prevail on claim 11 on this asserted ground of unpatentability.

1. Matsuda

Matsuda, titled “Compound Having Affinity Substance to Antibody and Biorthogonal Functional Group, or Salt Thereof,” provides “novel techniques enabling modification of an antibody, particularly regioselective modification of an antibody.” Ex. 1011, code (54), ¶ 8. Matsuda observes that “when the number of bonds and the bond positions of a drug of an ADC are changed, pharmacokinetics, and a releasing rate and effects of the drug change” and notes that “next-generation ADCs are required to control the number and positions of a drug to be conjugated.” *Id.* ¶ 4. Matsuda states that “when the number and positions are fixed, the problems of expected

efficacy, variations in conjugation medicines, and lot difference, or what is called regulation, will be solved.” *Id.*

2. *Reasons to Combine & Reasonable Expectation of Success*

Petitioner argues that, as shown in the obviousness analysis of grounds 3 and 5, *supra*, “Yamada discloses an antibody regioselectively modified with a bio-orthogonal function group at position 248 represented by (Formula (IV)).” Pet. 83 (citing various portions of Ex. 1002 and Ex. 1009). Petitioner argues that “Yamada provides motivation for a POSA to prepare an antibody regioselectively modified with a bio-orthogonal functional group at the lysine residue at position 248” and “explains prior ADC production methods result in nonuniformity and varying DARs.” According to Petitioner, because “[t]he DAR can impact a variety of pharmacokinetic parameters, . . . a POSA would be motivated to regioselectively modify an antibody to prepare consistent DARs.” *Id.* at 77 (citing Ex. 1005 ¶ 4, Ex. 1002 ¶ 421, Ex. 1027, pg. 541). Petitioner also argues that “Matsuda provides further motivation for a POSA to regioselectively modify an antibody at lysine 248 according to claim 1.” Pet. 78; *see also* Ex. 1002 ¶ 421, 422. Petitioner argues that “[a] POSA would need only make selections of disclosed substituents for Formula (IV) as shown in the flow charts below to arrive at the first and third structures of claim 11.” Pet. 81–83; *see also* Ex. 1002 ¶ 449 (stating that “there are two ways in which Formula (IV) can be completed to arrive at the first and third structures of claim 11”). Dr. Tumey states that “the first and third structures recite[d] in claim 11 of the ’675 Patent are disclosed in Yamada and could be predictably constructed based on Yamada’s disclosure.” Ex. 1002 ¶ 451.

Patent Owner argues that Petitioner fails to provide a motivation or a reason as to why a skilled artisan would have combined the references

because “Petitioner mentions some iteration of ‘motivation’ only five times” and “only eight times” in the testimony by Dr. Tumey. Prelim. Resp. 12 (citing Pet. 4, 77, 78, 79; citing Ex. 1002 ¶¶ 60, 61, 62, 403, 421, 422).

Patent Owner argues that Petitioner’s proposed combination is solely based on impermissible hindsight. *Id.* at 14. Patent Owner argues that Dr. Tumey’s “near-verbatim recitation of the Petition” is neither persuasive nor helpful. *Id.* at 13. Patent Owner argues that Petitioner’s “conclusory assertion does not explain why a POSA would have had a reasonable expectation of success, nor does it address any technical challenges or compatibility concerns associated with the proposed combination.” *Id.* at 17.

As discussed previously, Patent Owner’s argument regarding the purported frequency with which Petitioner and/or Dr. Tumey uses phrases such as “motivation to combine” (*see* Prelim. Resp. 12) does not rebut Petitioner’s testimonial and other evidence in support of Petitioner’s argument regarding motivation.

For example, Dr. Tumey testifies that as of 2019, “there was an expectation that site-specific conjugation would decrease off-target toxicity and improve the pharmacokinetic properties of the ADC, and thus there was a clear motivation in the art to pursue technologies that allowed site-specific conjugation.” Ex. 1002 ¶ 60 (citing Ex. 1027, 538); Ex. 1027.

Dr. Tumey also testifies that “those working in the field of ADCs were motivated to devise means for selectively modifying antibodies at particular sites in order to preserve the antibody’s functions and to achieve more consistent DAR values” and that “it was firmly established before March 2019 that the conjugation site on the antibody component, a well-defined DAR, and homogeneity of the ADC product were important parameters that need to be considered in ADC development, and individuals

of ordinary skill in the art had every incentive to develop methodologies that would allow for more predictable and defined ADC production.” Ex. 1002 ¶ 63 (citing Ex. 1028, S101–S105; Ex. 1029, 1, 13–14); Ex. 1028; Ex. 1029.

Dr. Tumey testifies that Yamada “provides motivation for a POSA to prepare an antibody regioselectively modified with a bio-orthogonal functional group at the lysine residue at position 248.” Ex. 1002 ¶ 421.

Dr. Tumey testifies that “Yamada discloses an antibody modified at lysine residue 248 to include a bio-orthogonal click chemistry function group, including a terminal azide group” whereas Matsuda similarly “discloses an antibody modified at lysine residue 248 to include a bio-orthogonal click chemistry functional group, including a terminal azide and a terminal maleimide. *Id.* ¶¶ 424, 425. Dr. Tumey testifies that “[t]he DAR of an ADC can influence its stability, solubility, antigen binding, clearance and biodistribution, resulting in different DAR species having distinct pharmacokinetics behaviors.” *Id.* ¶ 421 (citing various portions of Ex. 1005 and Ex. 1027). Based on these prior art teachings, Dr. Tumey concludes that “a person of ordinary skill would be motivated to regioselectively modify an antibody in order to prepare ADCs with a known and consistent DAR so that the pharmacokinetic properties of the ADC can be consistent.” Ex. 1002 ¶ 421. Dr. Tumey testifies that “Matsuda provides further motivation” because “Matsuda discloses lysine 248 as one of only five preferred positions” and “demonstrates that antibodies can be regioselectively modified with a terminal azide as a bio-orthogonal functional group (Example 5-2-1) and a terminal azide as a terminal bio-reactive functional group (Example 5-2-2).” *Id.* ¶ 422 (citing various portions of Ex. 1011). Dr. Tumey testifies that “Matsuda discloses modification of lysine residue

248 is preferable.” *Id.* ¶ 428 (citing Ex. 1011 ¶ 146); *see also id.* ¶ 429 (citing Ex. 1011 ¶ 329).

Dr. Tumey provides a flow diagram showing how “a POSA could readily envisage that the first and third structures recited in claim 11 by selecting the components of Formula (IV)” in Yamada. Ex. 1002 ¶¶ 450–451 (citing Formula IV in Ex. 1009); *see also* Ex. 1002 ¶¶ 445–449 (citing various portion in Ex. 1009 including teachings regarding Formula (IV)); Pet. 80–83. We credit Dr. Tumey’s testimony regarding a POSA’s motivation to combine Yamada and Matsuda with a reasonable expectation of success.

Based on our review and consideration of the current record, we are persuaded that Petitioner has adequately shown for purposes of institution that there is sufficient rationale to combine as well as a reasonable expectation of success in combining the teachings of Yamada and Matsuda in the manner suggested.

3. Analysis of Ground 7b

Petitioner argues that the combined teachings of Yamada and Matsuda teach or suggest all elements of claim 11. Pet. 69–76, 77–79, 80–83.

At this stage of the proceeding, Patent Owner does not address Petitioner’s specific contentions with respect to the elements of claim 11. *See generally* Prelim. Resp. Based on our review and consideration of the current record, we determine that Petitioner has sufficiently shown that the combination teaches all elements of claim 11 for purposes of institution.

4. Conclusion Regarding Ground 7b

Based on the reasons provided *supra*, we determine that the information presented in the Petition demonstrates a reasonable likelihood

that Petitioner will prevail as to its contentions that claim 11 would have been unpatentable under 35 U.S.C. § 103 in view of Yamada and Matsuda.

IV. CONCLUSION

After considering the evidence and arguments presented in the Petition and the Preliminary Response, we determine Petitioner has established a reasonable likelihood of prevailing on its assertion that the sole remaining claim 11 of the '675 patent would have been unpatentable, and we institute an *inter partes* review of claim 11 on all grounds (grounds 1, 3, 5, 7a, and 7b) presented in the Petition. *See* 37 C.F.R. § 42.108(a).

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314, *inter partes* review is instituted as to claim 11 of the '675 patent and on all grounds presented in the Petition as to claim 11; and

FURTHER ORDERED that *inter partes* review is commenced on the entry date of this Order, and 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.

IPR2025-00283
Patent 11,896,675

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