

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AJINOMOTO CO., INC.

Petitioner,

v.

ABTIS CO., LTD.

Patent Owner.

CASE: IPR2025-00283

U.S. PATENT NO. 11,896,675

PATENT OWNER'S NON-CONTINGENT MOTION TO AMEND UNDER
37 C.F.R. § 42.121

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TABLE OF PATENT OWNER EXHIBITS

Exhibit No.	Description
2001	Statutory Disclaimer of U.S. Patent No. 11,896,675
2002	U.S. Patent App. No. 18/154,998
2003	U.S. Patent App. No. 16/980,503
2004	Declaration of Dr. Zhaohui Sunny Zhou
2005	<i>Curriculum Vitae</i> of Dr. Zhaohui Sunny Zhou
2006	Deposition Transcript of Dr. Lawrence Nathan Tumey

I. INTRODUCTION

Patent Owner AbTis Co., Ltd. (“AbTis”) is forgoing a Formal Response, unconditionally filing this Motion to Amend (“MTA”) to substitute the claims as set forth in the claim listing found in Appendix A, and asking the Board to decide the patentability of the claims as so substituted. *See* 37 C.F.R. § 42.221 (“[T]he Board may exercise its discretion to grant or deny a motion to amend or raise a new ground of unpatentability in connection with a proposed substitute claim.”).

Patent Owner previously submitted a statutory disclaimer for claims 1-10, 12, and 13. Ex. 2001. Patent Owner now requests that original claim 11 be canceled and that proposed substitute claims 14-16 (collectively, the “Proposed Substitute Claims”) be entered. Because canceled claim 11 is a dependent Markush-type claim covering three specific chemical moieties, the three corresponding substitute claims (each directed to one of the three chemical moieties) constitute a reasonable number of narrower substitute claims, particularly given that Patent Owner already disclaimed twelve other claims in the ’675 Patent.

As explained further below, the Proposed Substitute Claims satisfy the requisite showing for a motion to amend. Support for each of the Proposed Substitute Claims from “the original disclosure of the patent” and from the “earlier-filed disclosure for each claim for which benefit of the filing date of the earlier-filed disclosure is sought” is provided below. *See* 37 C.F.R. §§ 42.121(b)(1)-(2).

Additionally, the proposed claim amendments (1) present a reasonable number of substitute claims; (2) do not impermissibly enlarge the scope of the claims; (3) do not introduce new subject matter; and (4) respond to a ground of unpatentability in the trial.

II. MTA ELECTION/REQUEST

Patent Owner elects preliminary guidance from the Board for this MTA.

III. PROPOSAL MEETS REQUIREMENTS FOR AMENDMENT

A. Patent Owner Proposes a Reasonable Number of Substitute Claims

Patent Owner's proposed modifications consist of three substitute claims, proposed substitutes 14-16, for canceled dependent claim 11, which depends directly from disclaimed independent claim 1. Canceled claim 11 is directed to a Markush group of three specific chemical moieties. Proposed substitute claims 14-16 are independent claims, each directed to one of the specific chemical moieties of canceled claim 11. Given the nature of claim 11 as a Markush-type claim to three moieties, three replacement claims is "a reasonable number of substitute claims" as required by 35 U.S.C. § 316(d)(1)(B) and 37 C.F.R. § 42.121(a)(3). Further, although there is a rebuttable presumption that "one substitute claim will be needed to replace each challenged claim," the circumstances here warrant three substitute claims because AbTis has already disclaimed twelve claims in the same patent,

making the number of substitute claims less than one substitute per original claim. *See* 37 C.F.R. § 42.121(a)(3).

B. Proposed Substitutes Do Not Enlarge the Scope of the Claims

Proposed substitute independent claims 14, 15, and 16 merely separate the originally recited alternative chemical moieties into distinct species without expanding the overall claim scope. *Corning Optical Comm'n RF, LLC v. PPC Broadband, Inc.*, IPR2014-00441, Paper 19 at 3 (P.T.A.B. Oct. 30, 2014); Ex. 2004, ¶ 44. The Proposed Substitute Claims include all of the limitations of original dependent claim 11, which depends from disclaimed independent claim 1, but change two aspects of disclaimed claim 1 and original claim 11, resulting in narrower claim limitations. Ex. 2004, ¶¶ 45-46. Specifically, proposed substitute independent claims 14, 15, and 16 each (1) remove the negative limitation of disclaimed claim 1 incorporated into claim 11, and (2) replace the three-member Markush group of chemical moieties recited in original dependent claim 11 with an affirmative limitation specifying only one of those compounds. Removing the negative limitation does not constitute a broadening deletion, and affirmatively claiming each of the three chemical moieties separately further limits the scope of the Proposed Substitute Claims. Ex. 2004, ¶¶ 45-46; Ex. 2006, 80:8-81:3, 78:3-79:14.

i. The Proposed Substitute Claims Contain No Broadening Deletions

Patent Owner made no substantive deletions to the original limitations. *See* App'x A. Disclaimed claim 1 recited a negative limitation: “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.” As incorporated in dependent claim 11, that negative limitation was substantively superfluous because claim 11 recited three specific chemical compounds defined by their structures to the implicit exclusion of other structural features. Ex. 2004, ¶ 46.

Petitioner's own expert confirmed the negative limitation of disclaimed claim 1 is superfluous for original claim 11:

A. I can just say in my opinion as a chemist, I can look at Claim 11 and see what modified antibodies are encompassed by claim -- whether a modified antibody is encompassed by Claim 11 or not, merely by looking at Claim 11, without that language. . . .

Q. But from a scientific perspective, you can see what's in Claim 11 and what's not based on this structural description; *you don't need the Negative Limitation to determine the scope of the structures in Claim 11?*

A. That is correct.

Ex. 2006, 80:8-81:3 (objections omitted).

In other words, the structural limitations in original claim 11—and by extension in the proposed substitute claims—fully define the scope of the modified lysine residues, rendering the negative limitation unnecessary for original claim 11 and make substitute claims 14-16 squarely within the scope of original claim 11. Ex. 2004, ¶ 46.

Ultimately, Dr. Tumey’s testimony corroborates that removal of the negative limitation does not enlarge the claim scope. Rather, it eliminates redundant language while preserving (and narrowing) the precise structural definition of the claimed moiety. Ex. 2004, ¶ 46. Specifically, by removing the negative limitation, which permitted a wide range of other chemical moieties so long as they were not among those expressly excluded, the Proposed Substitute Claims now exclude all such unlisted possibilities and are limited to one of the three specific chemical moieties. Ex. 2004, ¶¶ 44-46. Notably, Dr. Tumey acknowledged that disclaimed claim 1 “recites a genus of modified antibody groups,” and the negative limitation is one of “the characteristics defining that group of compounds [] that it’s encompassing.” Ex. 2006, 75:7-14. Then, Dr. Tumey confirmed that the compounds, or chemical moieties, recited in original claim 11 do not include the characteristics of the negative limitation:

Q. [A] person of ordinary skill in the art would understand that these modified lysine structures in Claim 11, for example, don't have *terminal thiol groups*. Correct?

A. That's correct.

Q. And then you would also understand that the structures of Claim 11, just by looking at the structure of Claim 11, don't have the *terminal hydroxy group*; is that right?

A. Correct.

Q. [A] person of ordinary skill in the art would be able to determine that the compounds claimed in Claim 11 don't have a *terminal amino group*; is that right?

A. Correct.

Q. And the same would be true that the structures of Claim 11 don't include a *terminal aldehyde group*. Right?

A. Correct. . . .

Ex. 2006, 78:11-79:14.

Q. And the structures would not include a *terminal carboxyl group*. Correct?

A. Correct.

Id. at 111:20-22; *see also id.* at 79:16-80:16. By specifically reciting only one specific chemical moiety in each of the Proposed Substitute Claims, the new claims necessarily exclude all other chemical moieties that were originally contemplated by

original claim 1's negative limitation and are instead, limited only to the specific chemical moiety recited in proposed substitute claims 14 (azide), 15 (norbornene), and 16 (norbornene).

The amended claims therefore comply with 35 U.S.C. § 316(d)(3) and 37 C.F.R. § 42.121(a)(2)(ii), as they are not broader than the original claim.

ii. The Proposed Substitute Claims Only Have Further Limiting Amendments

The Proposed Substitute Claims are limited to one of three specific chemical moieties that were included in a Markush group of original claim 11. Specifically, substitute claim 14 affirmatively recites the chemical moiety azide with an ether-containing spacer group, substitute claim 15 affirmatively recites the chemical moiety norbornene with no spacer group, and substitute claim 16 affirmatively recites the chemical moiety norbornene with an ether-containing spacer group. Ex. 2004, ¶ 52.

Because proposed substitute claims 14, 15, and 16 are now each expressly limited to one supported compound and no longer encompass the negative limitation (disclaimed original claim 1) and Markush group (original claim 11), each claim is narrower in scope than original claim 11. *See Int'l Flavors & Fragrances Inc. v. United States Dep't of Agric.*, IPR2013-00124, Paper 12 at 9 (P.T.A.B. May 20, 2014) (finding "[n]o broadening of scope" where proposed independent claim added

“an additional Markush group limitation specifying the isolongifolenone analogs that may be used in the claimed method” because proposed claim “limits the analogs used in the method to the first five compounds of original dependent claim 8”). In other words, while original claim 11 could be met by any one of the three chemical moieties, proposed substitute claims 14, 15, and 16 require an azide, a norbornene with no spacer group, and norbornene with an ether-spacer group, respectively.

Therefore, all amendments of the Proposed Substitute Claims are further limiting, and Patent Owner does not seek to enlarge the scope of the claims.

C. There Is Written Description Support for Each Substitute Claim

None of the Proposed Substitute Claims introduces new subject matter because each of the Proposed Substitute Claims is supported by the specification for the originally filed 18/154,998 Application (the “’998 Application”) (Ex. 2002) that issued as the ’675 Patent, and the ’675 Patent’s Parent Application, Application Ser. No. 16/980,503 (the ’503 Application) (Ex. 2003). Ex. 2004, ¶¶ 47-52.

The Proposed Substitute Claims each specify a particular chemical structure that was previously included in a three-member Markush group in original claim 11, and removes the broad negative limitation of disclaimed claim 1. Ex. 2004, ¶¶ 47-52.

As a preliminary matter, Petitioner has effectively conceded that the Proposed Substitute Claims are entitled to at least the September 14, 2020 priority date of the

'503 Application: “The '675 Patent and the '959 Publication share essentially identical specifications.”¹ Petition, 22; *see, e.g., id.* at 29-37 (arguing that the '959 Publication, which has a substantially identical specification to the '998 Application, discloses each element of original claim 11—now proposed substitute claims 14, 15, and 16). Petitioner raised a lack of written description issue for the negative limitation in claim 1, but did not raise any other written description deficiencies.

Accordingly, as Petitioner itself recognizes and as discussed further below, every limitation of original claim 11 and proposed substitute claims 14-16 is supported by both the '998 and '503 Applications—each of which contains “essentially identical” specifications to the '959 publication that Petitioner relied on to allege anticipation of the '675 Patent. Petition, 30.

Exemplary support for the amended claims from the original applications for all proposed substitute claim limitations is provided in the table below. *See Lectrosonics, Inc.*, IPR2018-01129, -01130, Paper 15 at 7-8 (P.T.A.B. Feb. 25, 2019); 37 C.F.R. §§ 42.121(b)(1)-(2).

¹ Patent Owner reserves the right to dispute Petitioner’s assertion that the '959 Publication is entitled to a priority or publication date of September 17, 2020.

<u>Claim</u>	<u>'998 Application</u>	<u>'503 Application</u>
Proposed Substitute Claim 14		
14[pre]	[0008]-[0010], [0014]-[0017], [0232]-[0242], [0374]-[0413], [0572]-[0577], [0580], [0581], [0582]-[0587], [0590]-[0591], Figs. 21-22	[0007]-[0009], [0013]-[0016], [0231]-[0241], [0373]-[0412], [0571]-[0576], [0579], [0580], [0581]-[0586], [0589]-[0590], Figs. 21-22
14[a]	[0008], [0010], [0227], [0577], [0580]-[0581], [0585]-[0587], [0590]-[0591]	[0007], [0009], [0226], [0576], [0579]-[0580], [0584]-[0586], [0589]-[0590]
14[b]	[0008]-[0010], [0016], [0227], [0228], [0577], [0578], [0579], [0587], [0588], [0589], [1295]-[1298]	[0007]-[0009], [0015], [0226], [0227], [0576], [0577], [0578], [0586], [0587], [0588], [1294]-[1297]
14[c]	[0225], [0227], [0577], [0582]	[0224], [0226], [0576], [0581]
14[d]	[0013]-[0017], [0232]-[0249], [0395]-[0409], [0447]-[0452], [0575]-[0578], [0588], [0600]-[0606], [0980]-[0982], [1263], [1290]-[1294], [1318]-[1329], [1318]-[1329], Figs. 21-22, 48, 56-57	[0012]-[0016], [0231]-[0248], [0394]-[0408], [0446]-[0451], [0574]-[0577], [0587], [0599]-[0605], [0979]-[0981], [1262], [1289]-[1293], [1317]-[1328], [1317]-[1328], Figs. 21-22, 48, 56-57
Proposed Substitute Claim 15		
15[pre]	[0008]-[0010], [0014]-[0017], [0232]-[0242], [0374]-[0413], [0572]-[0577], [0580]-[0587], [0590]-[0591], Figs. 19 and 43	[0007]-[0009], [0013]-[0016], [0231]-[0241], [0373]-[0412], [0571]-[0576], [0579]-[0586], [0589]-[0590], Figs. 19 and 43
15[a]	<i>See Limitation 14[a]</i>	<i>See Limitation 14[a]</i>

15[b]	<i>See</i> Limitation 14[b]	<i>See</i> Limitation 14[b]
15[c]	<i>See</i> Limitation 14[c]	<i>See</i> Limitation 14[c]
15[d]	[0013]-[0017], [0232]-[0249], [0395]-[0409], [0452], [0575]-[0579], [0588]-[0589], [0938]-[0942], [0966]-[0968], [1162], [1254], [1282]-[1285], [1295]-[1298], Figs. 19, 42, 43, and 51-55	[0012]-[0016], [0231]-[0248], [0394]-[0408], [0451], [0574]-[0578], [0587]-[0588], [0937]-[0941], [0965]-[0967], [1253], [1281]-[1284], [1294]-[1297], Figs. 19, 42, 43, and 51-55
Proposed Substitute Claim 16		
16[pre]	[0008]-[0010], [0014]-[0017], [0232]-[0242], [0374]-[0413], [0572]-[0577], [0580], [0581], [0582]-[0587], [0590]-[0591], Figs. 15 and 17	[0007]-[0009], [0013]-[0016], [0231]-[0241], [0373]-[0412], [0571]-[0576], [0579], [0580], [0581]-[0586], [0589]-[0590], Figs. 15 and 17
16[a]	<i>See</i> Limitation 14[a]	<i>See</i> Limitation 14[a]
16[b]	<i>See</i> Limitation 14[b]	<i>See</i> Limitation 14[b]
16[c]	<i>See</i> Limitation 14[c]	<i>See</i> Limitation 14[c]
16[d]	[0013]-[0017], [0232]-[0249], [0395]-[0409], [0447]-[0452], [0575]-[0579], [0588]-[0589], [0938]-[0942], [0955]-[0957], [1208], [1273]-[1277], [1295]-[1298], Figs. 15, 17, and 40-41	[0012]-[0016], [0231]-[0248], [0394]-[0408], [0446]-[0451], [0574]-[0578], [0587]-[0588], [0937]-[0941], [0954]-[0956], [1207], [1272]-[1276], [1294]-[1297], Figs. 15, 17, and 40-41

D. The Proposed Amendments Respond to and Overcome the Grounds of Record

Patent Owner's proposed amendments in the Proposed Substitute Claims are responsive to the grounds of unpatentability because (1) the substantive amendments address the claim for which the Panel instituted trial, *see* Paper 16, and (2) the limitations are added specifically to more clearly render the patented invention non-obvious from the prior art, including the art cited in the Petition and Institution Decision. The Petitioner bears the burden of establishing the unpatentability of the amended claims. *See Aqua Prods., Inc. v. Matal*, 872 F.3d 1290, 1327-28 (Fed. Cir. 2017) (en banc); 37 C.F.R. § 42.121(d)(2). Nonetheless, Patent Owner's claim amendments overcome the asserted grounds of unpatentability as discussed below.

The grounds of rejection for which the *inter partes* review was granted are based on one or more of the following references (referred to collectively herein as "the cited references"): CA 3132959A1 (the "'959 Publication"; Ex. 1005); PepTalk Poster (Ex. 1006), PepTalk Presentation (Ex. 1007); WO 2018/199337 ("*Yamada*"; Ex. 1009); and WO 2019/240288 ("*Matsuda*"; Ex. 1011). Substitute claims 14, 15, and 16 are patentable over the cited references.

i. Proposed Substitute Claims 14, 15, and 16 Are Entitled to a Priority Date of at Least September 14, 2020, Rendering Petitioner’s Arguments That Original Claim 11 Is Obvious over the ’959 Publication Moot (Ground 1)

The ’959 publication claims priority to the same provisional application as the ’675 Patent: U.S. Provisional Patent App. No. 62/815,557, which was filed March 8, 2019. The earliest non-provisional application leading to the ’675 Patent was filed on September 14, 2020, and the ’959 publication allegedly published three days *later* on September 17, 2020. The ’959 publication therefore is not prior art to the proposed substitute claims under 35 U.S.C. § 102(a) because it was not published (September 17, 2020) before the effective filing date (September 14, 2020). The ’959 publication also is not prior art to the proposed substitute claims under 35 U.S.C. § 102(b) because the inventors are the same.

E. Grounds 3, 5, and 7: PepTalk Poster (Ex. 1006), PepTalk Presentation (Ex. 1007), WO 2018/199337 (“*Yamada*”; Ex. 1009) and/or WO 2019/240288 (“*Matsuda*”; Ex. 1011) Do Not Render Obvious the Proposed Substitute Claims

Petitioner relies on four references, PepTalk Poster, PepTalk Presentation, and *Yamada* and/or *Matsuda*, to challenge original claim 11 in each of Grounds 3, 5, and

7. *See* Petition, 2-3, 56, 68, 83.² But, the cited references do not render obvious the proposed substitute claims 14, 15, and 16.

Preliminarily, in each of grounds 3, 5, and 7, Petitioner relies on the *Yamada* reference that was before the examiner during prosecution. Petitioner has not shown any “material error” made by the USPTO during prosecution to satisfy its burden of proving that the ’675 Patent claims are unpatentable over *Yamada*. *See Adv. Bionics, LLC v. Med-El Elektromedizinische Geräte GMBH*, IPR2019-01469, Paper 6 (P.T.A.B. Feb. 13, 2020) (precedential). The examiner never rejected claim 11 over *Yamada* in allowing it. Rather, the examiner rejected *other* claims over *Yamada*, but ***did not reject the dependent claim that issued as claim 11***. Ex. 2035, at 322-331. The examiner only objected to that claim because it depended from a rejected independent claim. Ex. 1035, at 327. In response, AbTis amended the rejected claims on which claim 11 depended. Ex. 1035, at 302-313. Following those amendments, the examiner withdrew the rejection based on *Yamada* and allowed the claims. Ex. 1035, at 90-98. Thus, the U.S. Patent and Trademark Office (“USPTO”)

² While Petitioner relied on *Matsuda* to challenge certain claims in Grounds 3, 5, and 7, Petitioner never directly applied *Matsuda* in its challenges to original claim 11.

expressly considered *Yamada* and found the substance of claim 11 patentable over it, and narrower substitute claims 14-16 are likewise patentable.

The prosecution history underscores that the claimed compounds are structurally distinct from *Yamada*'s generalized conjugates and that the examiner's allowance was predicated on that distinction. *See* Ex. 2004, ¶ 83. Petitioner identified nothing in *Yamada* that the examiner, during prosecution, did not already consider.

Additionally, *Matsuda* (Ex. 1011) was of record during prosecution of the '675 Patent. Specifically, the examiner cited *Matsuda* in an Information Disclosure Statement, and *Matsuda* was listed on the face of the '675 Patent. *See* Ex. 1035, 108; Ex. 1001, Cover. Petitioner has not even attempted to establish any "material error" made by the USPTO during prosecution of the '675 Patent to satisfy its burden of proving that the '675 Patent claims are unpatentable over *Matsuda*. *See Adv. Bionics*, IPR2019-01469, Paper 6. This is, in part, because Petitioner failed to apprise the Board, in its Petition, that *Matsuda* was of record during prosecution of the '675 Patent. *See* Petition, 84 ("Matsuda w[as] not of record or considered by the Office during prosecution of the '675 Patent."). Petitioner also cannot show that the USPTO made a material error with respect to *Matsuda* because a POSITA would have understood *Matsuda* as teaching away from Petitioner's proposed combination with *Yamada* as discussed below in Section I.E.ii.

i. Petitioner Fails to Accurately Set Forth the State of the Art

As of the priority date, the antibody-drug conjugate (“ADC”) and site-specific protein modification field was complex, and by no means predictable. *See* Ex. 2004, ¶ 37. As antibody vehicles that carry drug molecules to cells, there are issues researchers faced. Petitioner’s expert explained that even a concept as straightforward as drug-to-antibody ratio (“DAR”), how many drug molecules each antibody should carry to the cells, “has been all over the map.” Ex. 2006 at 49:10-50:1. Some of the concerns included off-target toxicity, achieving adequate purity, immunogenicity, and achieving efficacy. *Id.* at 50:5-54:14. Against this backdrop, Patent Owner has invented the claimed compounds. While Petitioner’s Grounds allege that the claimed compounds are obvious based on certain prior art references, Petitioner fails to provide any direction, motivation, or reasonable expectation of success in digging through the billions of possible compounds generically disclosed in the prior art and attaining the claimed compounds.

ii. Petitioner’s Ground 7 References, WO 2018/199337 (“Yamada”; Ex. 1009) and WO 2019/240288 (“Matsuda”; Ex. 1011) Do Not Render Obvious the Proposed Substitute Claims

Substitute claims 14-16 are patentable over the Ground 7 references, *Yamada* and *Matsuda*. *Yamada* does not disclose the antibodies with modified lysine residues of the claims, so Petitioner impermissibly uses hindsight to begin from the

claims and work backward through the billions of compounds disclosed in *Yamada* to assert obviousness. Ex. 2004, ¶¶ 84-85. But Petitioner provides no reason to choose any one of the functional groups in the claims from among the billions in *Yamada*, let alone all of them at once. *Id.* at ¶ 86.

First, Petitioner's argument mischaracterizes *Yamada*'s disclosure. Ex. 2004, ¶¶ 98-103. Formula (IV) in *Yamada* (L1-B-R'-T) is a schematic representation of a generalized conjugate, not a structural definition of any specific linker or compound. Ex. 2004, ¶¶ 83, 99. *Yamada* does not disclose any of the modified lysine residues of the substitute claims. Ex. 2004, ¶ 96. Rather, Petitioner relies on *Yamada*'s disclosure of upwards of billions of possible compounds to be the claimed compounds of original claim 11. Ex. 2004, ¶¶ 90-92. This is improper hindsight. *See In re Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965) ("It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.").

Petitioner's expert's "Option 1" diagram is precisely the sort of litigation-created reconstruction assembled solely to meet the compounds claimed in original claim 11 that the case law does not permit. *See, e.g.*, Ex. 1002, ¶ 450; Ex. 2004, ¶¶ 91-93. Petitioner cites to various independent passages throughout the 186-

page specification to cherry-pick individual substituent definitions and variables that were never presented together in *Yamada*. Ex. 2004, ¶¶ 98-101. For example, to define Formula (IV), Petitioner identifies ¶¶ [0626]-[0627] as defining “L1”; identifies ¶ [1510] as defining “R”; and points to ¶¶ [0616]-[0618], [0619]-[0624], [0627], [0631]-[0639] for support of Petitioner’s “Option 1,” which purportedly discloses the “first and third structures of [original] claim 11.” Petition, 50-52. The law is clear that disparate definitions cannot be stitched together post hoc to create an undisclosed compound. *See In re Arkley*, 455 F.2d 586, 587 (C.C.P.A. 1972) (explaining that a disclosure must “direct those skilled in the art to the [invention] without *any* need for picking, choosing, and combining various disclosures[.]” (emphasis in original))

Yamada does not identify any preference, advantage, or motivation to choose the claimed options from among the many disclosed, let alone a reasonable expectation of success in doing so. Ex. 2004, ¶ 94. For example, there is no teaching in *Yamada* or another reference that an ether-containing spacer group of substitute claims 14 and 16 should be used, or that the chosen arrangement would confer any benefit over other spacer variants. Ex. 2004, ¶¶ 94-97; Ex. 2006 at 174:16-175:3 (Q: You don’t provide any prior art to make the ether link in the chain. Correct? In that spacer? A. *Within this document, I did not provide -- again, to my recollection - - any references of why we would make an ether over something else. But I did*

explain a little bit ago why intuitively, as a chemist, that I would.) (objections omitted). Moreover, there is no teaching that the very short spacer group of claim 15 would confer any benefit over other spacer variants. Ex. 2006 at 175:5-13 (Q. Okay. And then the same thing for no linker. Right? There's the bond from the carbonyl to the norbornene group, the second structure, Claim 11. You don't provide any reason – any prior art that gives a reason to do that. Right? A. *I did not provide any prior art in that document providing a reason for that, that is correct.*). Absent such guidance, selecting the exact combination recited in claim 11 (and now in the Proposed Substitute Claims) requires impermissible hindsight—relying on the claimed invention itself to know which elements to choose. *See Metalcraft of Mayville, Inc. v. The Toro Co.*, 848 F.3d 1358, (Fed. Cir. 2017) (“we cannot allow hindsight bias to be the thread that stitches together prior art patches into something that is the claimed invention.” (citing *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007))). This is highlighted by the ether spacer of claims 14 and 16, which Petitioner's expert, Dr. Tumey, admitted is not exemplified in *Yamada* or any other prior art reference he cited. Ex. 2006, 190:13-14 (“Well, since within [*Yamada*], I don't see any ethers there.”). Instead, Petitioner's expert relied on “intuition” and “operat[ing], kind of, [by] Occam's razor” to start with a “simple combination of things” and get to the claimed compound—this is not supported by any prior art, and

does not provide a clear reason to consider pursuing the claimed compounds, let alone render them obvious. Ex. 2006 at 145:22-149:14.

Moreover, Dr. Tumey said that all of the bioorthogonal groups disclosed in *Yamada* would be reasonable choices without stating any reason to choose the azide or norbornene of the substitute claims over any other. Ex. 2006, 155:6-156:16. Even though he asserted that norbornene was a proven click-chemistry functionality, Petitioner's expert did not, and could not, name its click-chemistry reaction partner. Ex. 2006 at 135:13-136:17. The Petition provides no reason that a POSITA would select the bioorthogonal groups on the claimed compounds from among available options.

In addition, Petitioner's entire analysis of *Yamada's* Formula IV is scientifically flawed, and could not produce the compounds of the claims because azide and norbornene cannot be produced by a cleavable linker L (cleaved to form L1) as Petitioner states. Ex. 2004, ¶¶ 98-105. *Yamada* Figure 2 provides a schematic of how each modified antibody is produced stepwise. See Ex. 1009, Fig. 2. Between Formula (II) and Formula (IV), *Yamada* discloses that L1 is a monovalent group formed by cleavage of a cleavable linker. Ex. 2004, ¶ 102. That means that for the claimed compounds to have L1 as their bioorthogonal group as Petitioner states, both azide and norbornene must be formed by cleaving another L group. Ex. 2004, ¶¶ 102-103. But Petitioner does not identify a group that can be cleaved to form

norbornene or azide, and its expert could not do so in his deposition, admitting that he did not provide a synthetic scheme for making the compounds he opined were obvious. Ex. 2006, 195:10-22; 205:5-14 (“Right, I do not have a synthetic scheme to make the compounds of Claim 11.”); Ex. 2004, ¶¶ 103, 105. Therefore, Petitioner fails to show that *Yamada* teaches the modified residues of the substitute claims are scientifically feasible, let alone that a POSITA would have reason to choose them. Ex. 2004, ¶ 105.

Even assuming a POSITA would have viewed *Yamada*’s Formula (IV) as an invitation to select among the many alternatives, the number of permutations is enormous: up to 13 billion possible variations. Ex. 2004, ¶¶ 84, 90-91, 97, 104. Each of L₁, B, R', for example, is independently variable, with *Yamada* listing dozens of potential atoms, groups, and chain lengths for all. Ex. 2004, ¶¶ 85-91, 99. The specific subset that would yield the claimed ether-linked D₁ spacer joined to a click-reactive group at lysine 248 represents one of many billions of theoretical combinations. Ex. 2004, ¶¶ 90-93.

Finally, the *Matsuda* reference that Petitioner cited against other claims teaches away from the beta heteroatom (ether oxygen) chain substituents of proposed substitute claims 14 and 16. Ex. 2004, ¶¶ 106-107. Petitioner cited *Matsuda* as part of a combination with *Yamada* to teach substitution of the antibody at the lysine 248 position. Petitioner failed to note when addressing claim 11,

however, that *Matsuda* teaches away from using beta heteroatom chains in the lysine 248 residue, specifically including an ether oxygen of the claimed compounds. Ex. 2004, ¶ 106. *Matsuda* discloses two such compounds, compound 26 and compound 60. ¶¶ [1014], [1023]. It further discloses that the antibody modification reactions did not progress with either beta-heteroatom compound 26 or compound 60. Ex. 1011, ¶¶ [1150]-[1152]; Ex. 2004, ¶ 107. In both cases, *Matsuda* discloses that the antibody modification reaction “had not progressed,” even after extended incubation at physiological temperature. Ex. 1011, ¶¶ [1150]-[1152]; Ex. 2004, ¶ 107. By contrast, *Matsuda* teaches that conjugation successfully proceeded when using analogs lacking the β -heteroatom (compounds 27–29). *Id.* ¶ [1152]; Ex. 2004, ¶ 107. Thus, *Matsuda* directly identifies the presence of a β -heteroatom as the structural feature responsible for failed antibody modification. Ex. 2004, ¶¶ 107-109.

Matsuda’s disclosure unambiguously teaches away from the β -heteroatom-containing (ether-linked) D₁ spacers recited in proposed substitute claims 14 and 16. Ex. 2004, ¶ 109. Specifically, a POSITA would have understood *Matsuda* to discourage such structures, recognizing that introducing an ether-oxygen atom at the β -position would have stereoelectronic effects that significantly reduces the rate of acylation by the lysine epsilon (ϵ)-amine. Ex. 2004, ¶ 109. Accordingly, *Matsuda* would have dissuaded a POSITA from modifying *Yamada*’s conjugates to include

the claimed β -heteroatom ether linkage—precisely the opposite of what Petitioner alleges. Ex. 2004, ¶¶ 109-110.

Even Petitioner’s own expert conceded that *Matsuda* “is teaching that there are problems with these two compounds,” and admitted that he “had not noticed that those two examples did not work” when drafting his declaration (Ex. 1002). *See* Ex. 2006, 184:4-19. Further, Petitioner’s expert explained that *Matsuda*’s disclosure is “certainly saying it did not give the desired full action that they were hoping for or anticipating.” Ex. 2006, 183:7-10.

In other words, the record shows that Petitioner’s combination of *Yamada* and *Matsuda* is self-contradictory: *Yamada* provides only generic schematic formulae with no direction to select an ether-linked spacer, while *Matsuda* expressly reports that β -heteroatom (ether) linkers do not work. Ex. 2004, ¶ 110. Far from motivating a POSITA to arrive at the claimed azide- and norbornene-modified lysine residues, *Matsuda* would have discouraged that modification path altogether. *See Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1305 (Fed. Cir. 2015) (explaining that the prior art teaches away when “a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant” (quoting *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994))); Ex. 2004, ¶¶ 109-111.

iii. Petitioner’s Ground 3 and 5 References, WO 2018/199337 (“*Yamada*”; Ex. 1009), PepTalk Poster (Ex. 1006) and PepTalk Presentation (Ex. 1007) Do Not Render Obvious the Proposed Substitute Claims

Petitioner relies on the PepTalk Poster and PepTalk Presentation (collectively, the “PepTalk References”) in Grounds 3 and 5, respectively, together with *Yamada*. Using these references is a misguided attempt to suggest that Petitioner came up with the claimed technology before Patent Owner. Instead, the PepTalk References show that Petitioner went into the proverbial haystack and found lots of hay, while Patent Owner went in and found three needles that Petitioner was never close to seeing. The PepTalk Poster and PepTalk Presentation do not disclose compounds of the Proposed Substitute Claims because they are missing critical attributes. Ex. 2004, ¶¶ 55-58, 63, 69-72, 77. The PepTalk References do not disclose compounds with an ether spacer as required by substitute claims 14 and 16, or compounds with no spacer as in substitute claim 15. Ex. 2004, ¶¶ 59-62, 66, 73-76. Moreover, the PepTalk References also do not disclose compounds substituted with norbornene, as required in substitute claims 15 and 16. Ex. 2004, ¶¶ 64-68, 78-82. The only way Petitioner argues these are obvious is by using *Yamada* and hindsight to arrive at the claimed chemical moieties.

In fact, the PepTalk References would teach away from using the AJICAP technology they disclose in detail. That technology is the first generation, and the

PepTalk References disclose a second generation AJICAP technology to improve upon the first generation, and avoid some of its deficiencies. Ex. 2004, ¶ 67. The deficiencies and imminent obsolescence would steer a POSITA away from the first generation AJICAP technology.

As stated above for *Yamada*, Petitioner has identified nothing that discloses the compounds of the substitute claims, let alone teaches how or why a POSITA would obtain them among the millions of structural options in *Yamada*. Therefore, the Proposed Substitute Claims are not obvious, and are patentable over the references Petitioner cites. Ex. 2004, ¶¶ 68, 82. For at least these reasons, proposed substitute claims 14, 15, and 16 are patentable.

IV. CONCLUSION

For the foregoing reasons, Patent Owner respectfully requests that the Board grant this motion such that the '675 Patent is amended to cancel original claim 11 and to include corresponding substitute claims 14, 15, and 16.

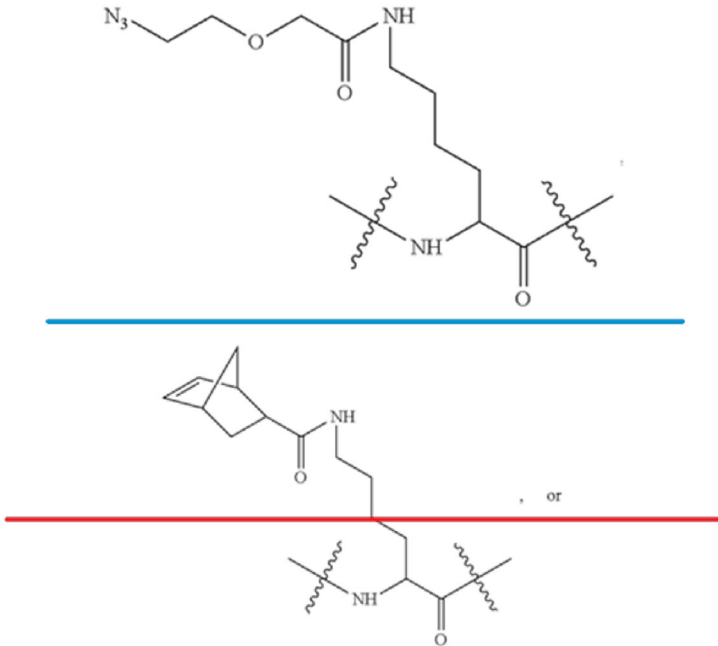
Dated: October 31, 2025

Respectfully submitted,

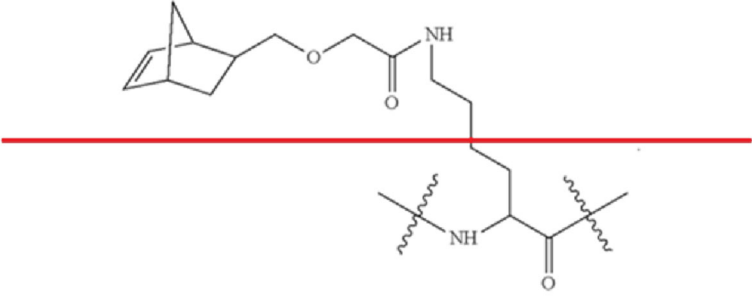
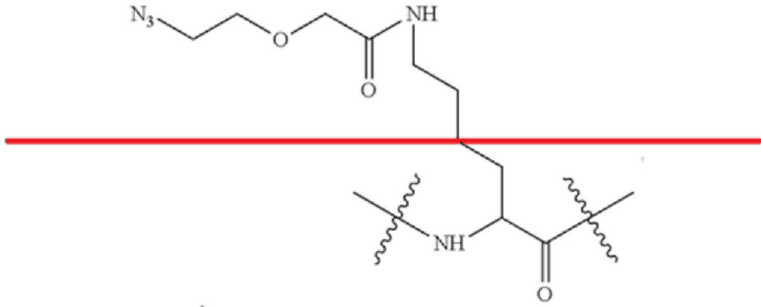
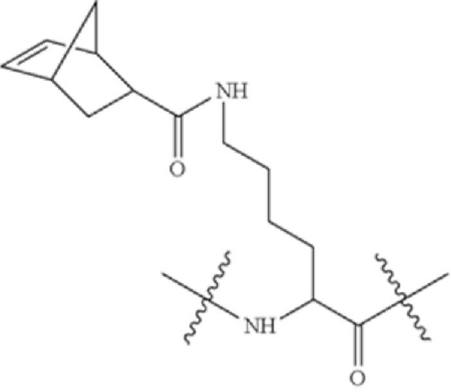
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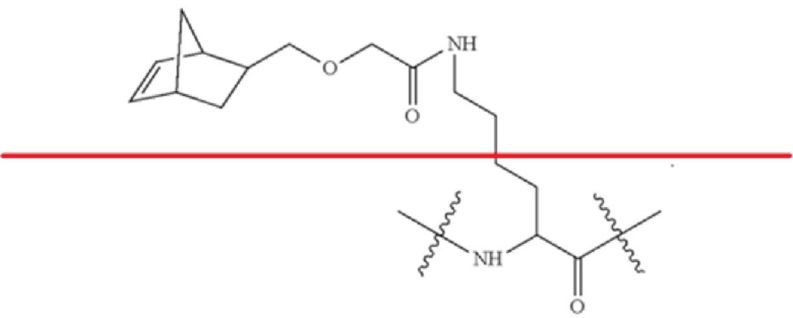
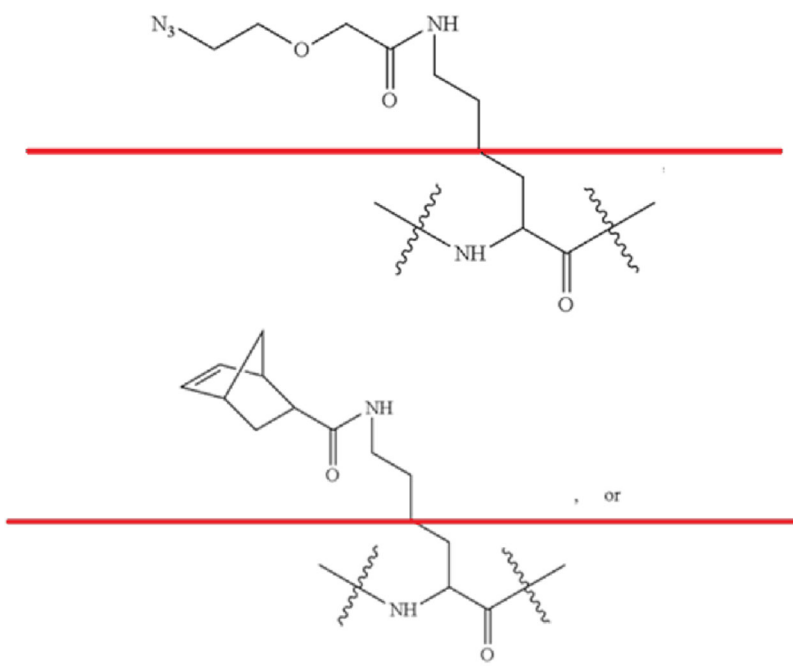
Counsel for Patent Owner

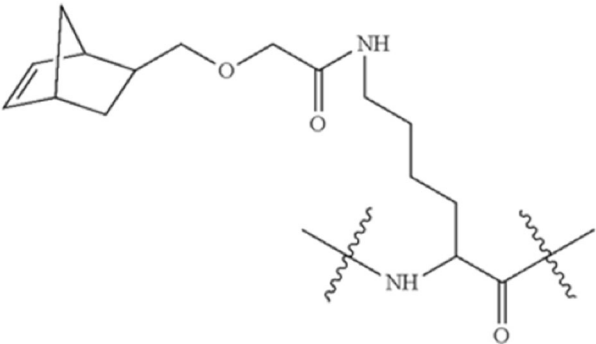
APPENDIX A
PROPOSED SUBSTITUTE CLAIM LISTING³

Claim	Limitation
14 <pre>[pre]</pre>	14. (proposed substitute for claim 11) ~~[[The]]~~ A modified antibody ~~of claim 1~~ <u>comprising a bio-orthogonal click chemistry functional group,</u>
14[a]	<u>wherein the modified antibody comprises one or more modified heavy chain,</u>
14[b]	<u>wherein each of the modified heavy chain comprises a modified lysine residue at 248 position of heavy chain amino acid sequence,</u>
14[c]	<u>wherein the 248 position is determined by an EU numbering system, and</u>
14[d]	wherein the modified lysine residue has following structure: 

³ Patent Owner shows deletions from the original claim with red brackets or red strikethroughs and additions with blue underlined text.

Claim	Limitation
	
15 <pre>[pre]</pre>	15. (proposed substitute for claim 11) ~~[[The]]~~ A modified antibody ~~of claim 1~~ comprising a bio-orthogonal click chemistry functional group.
15[a]	<u>wherein the modified antibody comprises one or more modified heavy chain,</u>
15[b]	<u>wherein each of the modified heavy chain comprises a modified lysine residue at 248 position of heavy chain amino acid sequence,</u>
15[c]	<u>wherein the 248 position is determined by an EU numbering system, and</u>
15[d]	wherein the modified lysine residue has following structure:  , or 

Claim	Limitation
	
16 <pre>[pre]</pre>	16. (proposed substitute for claim 11) ~~[[The]]~~ A modified antibody ~~of claim 1~~ comprising a bio-orthogonal click chemistry functional group.
16[a]	wherein the modified antibody comprises one or more modified heavy chain,
16[b]	wherein each of the modified heavy chain comprises a modified lysine residue at 248 position of heavy chain amino acid sequence,
16[c]	wherein the 248 position is determined by an EU numbering system, and
16[d]	wherein the modified lysine residue has following structure: 

Claim	Limitation
	 The chemical structure shows a norbornene ring (bicyclo[2.2.1]hept-2-ene) connected at the 3-position to a -CH₂-O-CH₂- group. This is followed by a carbonyl group (C=O) attached to an NH group. A four-carbon chain then connects this NH to another NH group. This second NH is attached to a carbon atom which is also bonded to a wavy line and a ketone group (C=O). The ketone is further attached to another carbon atom bonded to a wavy line. A horizontal blue line is positioned below the structure.

CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that the foregoing Motion to Amend, exclusive of the exempted portions as provided in 37 C.F.R. § 42.24(a), contains no more than 25 pages and therefore complies with the limitations of 37 C.F.R. § 42.24(a).

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CERTIFICATE OF SERVICE

I hereby certify that on October 31, 2025, a true and correct copy of the foregoing was caused to be served by filing this document through the PTAB's P-TACTS Filing System as well as delivering a copy via electronic mail on the following counsel of record for Petitioner at the following address:

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