

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SYNAFFIX B.V.,
Petitioner

v.

HANGZHOU DAC BIOTECH CO., LTD.,
Patent Owner

IPR2022-01531
Patent No 10,131,682

PATENT OWNER'S PRE-INSTITUTION SUR-REPLY

I. INSTITUTION SHOULD BE DENIED UNDER 35 U.S.C. § 325(D)

It is undisputed that Morales-Sanfrutos, Straus, and Singh were before the PTO. POPR at 26; Reply (“PR”) at 3. Contrary to the unsupported assertion that these references were “never applied against the claims” of the ’682 Patent, the Examiner considered each reference. PR at 3; EX. 2033; *Benitec Biopharma Ltd. v. Cold Spring Harbor Lab.*, IPR2016-00014, Paper 7 at 10 (P.T.A.B. Mar. 23, 2016) (“An Examiner’s initials on an IDS form ‘provides . . . a clear record in the application to indicate which documents have been considered by the examiner in the application.’”). Petitioner fails to describe any material error committed by the PTO in its evaluation of these references. Under the *Advanced Bionics* framework, the Board should exercise its discretion to deny institution. POPR at 23-24.

The Board has repeatedly denied institution under § 325(d) even if the particular reference in question was not directly addressed before. *See, e.g., R.J. Reynolds Vapor Co. v. Fontem Holdings 1 B.V.*, IPR2018-00626, Paper 7 at 19-21 (P.T.A.B. Sept. 27, 2018); *Gardner Denver, Inc. v. Utex Indus., Inc.*, IPR2020-00333, Paper 12 at 13-14 (P.T.A.B. Aug. 5, 2020) (denying institution where newly asserted references are “no more relevant ... than references that were presented during prosecution”). Newly asserted art and previously presented art do not need to “be identical or entirely cumulative, only ... substantially the same.” *Dropworks, Inc. v. Univ. of Chicago*, IPR2021-00100, Paper 9 at 13-14 (P.T.A.B. May 14, 2021).

Harris, Snow, and Petitioner's arguments regarding these references are identical or substantially similar to Lees, which was overcome during prosecution. POPR at 25-27. Petitioner now seeks a redo of the Patent Office's findings without any evidence that the Examiner erred in a material way. For the first time in the PR, Petitioner argues that Harris and Snow are not cumulative of Lees because the Examiner discussed Lees' heterobifunctional sulfone linker, but not Lees' homobifunctional sulfone linker in an Office Action. PR at 1-2; EX. 2025. Petitioner failed to proactively identify this in its Petition, which diminishes any showing of material error by the PTO. *Albany Int'l Corp. v. Kimberly-Clark Worldwide, Inc.*, PGR2021-00019, Paper 22 at 15-17 (P.T.A.B. June 22, 2021).

Petitioner argues that the Examiner failed to fully consider Lees' homobifunctional sulfone linker that DAC identified. PR at 2; POPR at 25. Yet Lees disclosed this structure multiple times and makes frequent reference to homobifunctional sulfones throughout. EX. 2026 at 18:10-16, 20:10-19, Fig. 1(b). Lees also discloses another homobifunctional sulfone structure. EX. 2026 at 20:20-21:12; 30:16-31, 32:13-14, Fig. 3(c). Nothing in the record suggests that the Examiner was unaware of these disclosures or that the reference was not substantively considered. It is more likely that the Examiner did not consider the homobifunctional structure to anticipate or render obvious the claimed inventions. *Advanced Bionics* instructs that "[i]f reasonable minds can disagree regarding the

purported treatment of the art or arguments, it cannot be said that the Office erred in a manner material to patentability.” *Advanced Bionics*, IPR2019-01469, Paper 6 at 9 (P.T.A.B. Feb. 13, 2020) (precedential).

Petitioner’s argument that it uses Harris and Snow for more than just the disclosure of the homo- and heterobifunctional sulfones (PR at 2), mischaracterizes the arguments in the Petition. Harris is a lead reference for Ground 2 (anticipation) and Ground 3 (obviousness), wherein these structures are the foundation of the arguments asserted in those Grounds. Pet. at 37-70; POPR at 49-52. Contrary to Petitioner’s framing, Harris discloses halo-ethyl sulfones as ***part*** of its homo- and heterobifunctional sulfone structures and the use of halo-ethyl instead of vinyl as a terminal substituent in these compounds is not a material distinction. EX. 1007, 19:24-30; Pet. 38; POPR 49-52. Also, Snow is used only as a secondary reference for dependent claims. The homo- and heterobifunctional sulfone compounds cited in Harris and Snow were substantively considered by the Examiner in Lees and overcome. Thus, the alleged additional disclosures do not weigh against denial here.

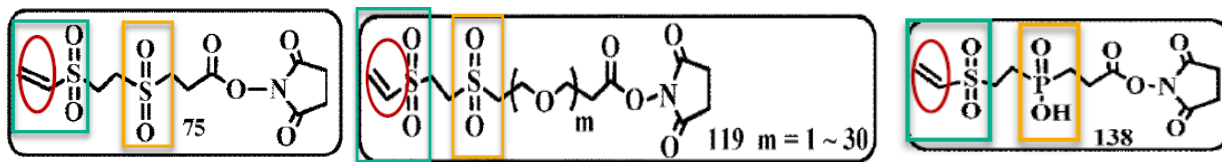
II. DAC’S PROPOSED CLAIM CONSTRUCTIONS ARE CORRECT

A. “Z”, “Y”, “Q” or “T”

Petitioner fails to offer any constructions for the “Z”, “Y”, “Q” or “T” terms and, instead, incorrectly contends that the specification and prosecution history of the ’682 Patent contradict DAC’s proposed constructions. But the plain language of

the claims and intrinsic evidence support DAC's proposals. POPR at 32-37. In addition, DAC's proposed constructions align with how a POSITA would understand the terms. Ex. 2001 ¶¶110-129. The PR does not demonstrate otherwise.

Petitioner argues that the specification discloses five compounds (55, 75, 99, 119, and 138) that allegedly contradict DAC's proposed constructions. PR at 2. But compounds 75, 119, and 138 do not contradict DAC's proposed constructions at least because those compounds do not disclose **a vinyl group alone** as Z. Rather, as depicted below, each of those compounds include **a vinyl sulfone** as Z (green rectangle) and a distinct sulfonyl or POOH group as Q (yellow rectangle).



Under DAC's proposal, the "Z" term should be construed as requiring that Z **independently enable** the reaction of the claimed linker. POPR at 34. As Petitioner admits, a vinyl group alone (as opposed to a vinyl that is part of a vinyl sulfone) does not have the ability to react with functional groups present in either cell-binding agents or cytotoxic drugs. POPR at 42. Thus, compounds 75, 119, and 138 (that have vinyl sulfones as Z, not vinyl alone) do not contradict DAC's constructions.

Compounds 55 and 99 also do not contradict DAC's proposed constructions, which are rooted in the plain language of the claims and the intrinsic evidence.

SIMO Holdings Inc. v. Hong Kong uCloudlink Network Tech. Ltd., 983 F.3d 1367, 1378-1379 (Fed. Cir. 2021) (distinguishing *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276-77 (Fed. Cir. 2008), on which Petitioner relies). In *SIMO*, the Federal Circuit explained that a court “must not allow [a] disclosed embodiment to outweigh the language of the claim, especially when the [] construction is supported by the intrinsic evidence.” *Id.* at 1379. Indeed, a claim need not cover all embodiments. *TIP Sys., LLC v. PBG, Inc.*, 529 F.3d 1364, 1373 (Fed. Cir. 2008).

Here, the plain language of the claims and intrinsic evidence dictates DAC’s proposed constructions. The claims demonstrate that both Y and Z are distinct components from Q and T (POPR at 32-37) and that it was the recitation of the independent Q and T structural spacer elements that led to the novelty of the Challenged Claims (*id.* at 4). The specification reiterates that Y and Z are structures that are specifically attracted to and independently reactive with certain chemical groups present on either a cell-binding agent or cytotoxic drug. *Id.* at 33-34, 36.

Moreover, DAC’s proposals do not exclude preferred embodiments. The specification discloses that, “[in] preferred embodiments, R1, R2, R3, and R4 are linear alkyl having from 1-6 carbon atoms, or polyethyleneoxy unit of formula $(\text{OCH}_2\text{CH}_2)_p$, $p=1\sim 100$.” Ex. 1001 at 9:8-10. Compounds 55 and 99 do not fall within the scope of these preferred embodiments and, therefore, should not weigh against DAC’s proposed constructions. *SIMO*, 983 F.3d at 1379 (“This case does

not present the issue of a construction that would exclude a *preferred* embodiment from a claim.”). The claim language and the intrinsic evidence support DAC’s constructions and outweigh Petitioner’s reliance on compounds 55 and 99.

The ’682 Patent’s file history also does not contradict DAC’s proposals. Petitioner contends that in response to the 3/8/18 Office Action (“OA”), DAC identified a vinyl alone as satisfying Z and, in response to the 6/12/20 Reexamination OA, similarly identified a vinyl alone as satisfying Y. PR at 6-7. Petitioner is wrong.

The Examiner in the 3/8/18 OA rejected the pending claims over a heterobifunctional linker structure in Lees, stating, “the NHS portion represents a functional group that enables reaction of the linker with a cell binding agent, and the vinyl group enables linkage of the linker to a cytotoxic drug.” Ex. 1018 at 42-43. In response, DAC ***repeated the Examiner’s mapping of Lees to the pending claim*** and then differentiated that claim from Lees based on the spacer element components (not the vinyl group) to overcome the rejection. *Id.* at 62. By repeating the Examiner’s argument, DAC did not adopt the Examiner’s characterization of Lees.

Petitioner’s reliance on DAC’s response to the 6/12/20 reexamination OA (PR at 6-7) is likewise misplaced. In response to a rejection by the Examiner over Govindan, DAC ***repeated the mapping of the structure the Examiner relied on*** because it “appeared [that the examiner] miss[ed] a portion of the proposed structure” and DAC stated that “[i]t is presumed that the following structure was

intended” *by the Examiner*. Ex. 1019 at 72. DAC argued that the structure did not correspond to the claimed invention “for at least” the reason that R2 as defined in the pending claim did not encompass a cyclic structure; where the structure relied upon by the Examiner did. *Id.* at 73. DAC did not identify vinyl alone as “Y”.

B. “cell-binding agent” (CBA)

CBA’s construction is governed by lexicography; it is defined in the specification as “[a] molecule that binds to, complexes with or reacts with a moiety *of a cell population sought to be therapeutically or otherwise biologically modified.*” POPR at 37-38. For the first time in its PR, Petitioner proposes that this term should mean “any agent that binds to, reacts with, or complexes with cells.” PR at 7. Petitioner, however, does not provide any evidence, intrinsic or otherwise, to support its position and, therefore, its construction should not be adopted.

Petitioner contends that the specification discloses numerous exemplary CBAs, which all may bind to a moiety on a cell population without necessarily targeting a specific cell population, but cites no evidence to support this proposition. *Id.* at 8-9. Petitioner seemingly raises the same argument that the claims must cover anything Petitioner deems a CBA within the specification. As discussed above, even if Petitioner’s characterization of the specification were correct, this is not the case. *See SIMO*, 983 F.3d at 1378-1379; *TIP Systems*, 529 F.3d at 1373 (patent claims “need not encompass all disclosed embodiments.”). Here, the inventor defined the

claimed CBA in terms of its ability to interact with specific cell-associated molecules that are intended to be targeted with the claimed linker conjugate. POPR at 37-38. The specification further discloses that “[i]n general monoclonal antibodies are preferred as a cell-surface binding agent if an appropriate one is available” (Ex. 1001 at 15:27-31) and that “[i]n certain preferred embodiments, the binding molecule for the conjugate in the present invention, can bind to both a receptor or a receptor complex expressed on an activated lymphocyte which is associated with an autoimmune disease” (*id.* at 23:52-56). This further supports that the claimed CBA has a ***specific target*** as opposed to indiscriminate binding capability.

Purportedly relying on *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997), Petitioner argues that DAC’s construction inserts an “intended use of the claimed conjugate . . . [that] has no such place in the claims.” PR at 7. But *Schreiber* is not directed to the issue of claim construction and is inapposite for how CBA should be construed. *GPNE Corp. v. Apple, Inc.*, No. 12-cv-02885-LHK, 2013 WL 4446819, at * 19 (N.D. Cal. Aug. 13, 2013) (stating that the issue raised in *Schreiber* related to patentability rather than claim construction). Moreover, the proposed CBA construction does not impute an intended use but rather informs, based on the express lexicography, the types of cell populations that a CBA should bind to, complex with, or react with.

Petitioner attempts to conflate DAC’s claim construction arguments with

DAC's rebuttal to Petitioner's anticipation arguments over Morales-Sanfrutos in view of Strauss. PR at 8. Petitioner contends that DAC's construction "suggests that binding must always occur under all conditions . . . [and that] no such limitations appear in the claims and none should be read into the claims." *Id.* But DAC never made these statements in the context of claim construction. Instead, regardless of how CBA is construed, Petitioner cannot show that the HRP disclosed in Morales-Sanfrutos is a CBA as that reference does not teach that HRP binds cells. Petitioner was thus forced to rely on Straus to argue that the missing element from Morales-Sanfrutos was "necessarily present" and "that it would be so recognized by persons of ordinary skill." *Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). DAC simply argued that Petitioner did not meet its burden because Straus does not disclose that HRP will "necessarily" (the inherent anticipation standard) bind to cells and did not show that a POSITA would recognize that alleged property of HRP. POPR at 46-48. In particular, Straus does not show that HRP necessarily or inherently binds to any particular kind of cell in the body (*in vivo*)—*e.g.*, cells that could be therapeutically targeted with a bioconjugate, such as an ADC. Ex. 2001 at ¶¶60-62. This is true regardless of claim construction.

III. HARRIS IS NOT ANALOGOUS ART

Harris is non-analogous art to the '682 Patent with respect to Grounds 3-5. While Petitioner argues that Harris is within the same field of endeavor (PR at 10),

it notably does not dispute DAC's assertion that Harris **does not** relate to the field of therapeutic protein-drug conjugates and **does not** teach conjugation of a drug to an antibody or other protein for use in therapeutic targeting. Petitioner improperly attempts to sidestep these points by stating that therapeutic targeting is an intended use of the Challenged Claims and should thus be ignored. *Id.*; see *Airbus S.A.S. v. Firepass Corp.*, 941 F.3d 1374, 1380-81 (Fed. Cir. 2019). The field of the '682 Patent relates to novel linkers that are desirable for the targeted treating of specific cell populations, such as cancer cells, using a selective cell-binding agent such as an antibody attached to a drug compound. See *e.g.*, Ex. 1001 at 1:6-15. Harris is silent as to these features and instead is focused on the use of PEG derivatives for "modifying the characteristics of surfaces and molecules" (Ex. 1007 at 3:2-6)—not for therapeutic targeting. Thus, Harris is not in the same field of endeavor.

Harris also does not address the same problem. The inventors of the '682 Patent were focused on developing therapeutic linkers that addressed the potency, selectivity, and pharmacokinetics of the resulting conjugates. POPR at 7. Harris does not disclose linkers designed to address these properties of therapeutic drug conjugates; indeed, Petitioner has presented no evidence to contradict this point.

IV. CONCLUSION

For the foregoing reasons, and those set forth in the POPR, the Board should deny institution of the Petition.

Date: July 19, 2023

By: /s/ Nick Cerrito

F. Dominic Cerrito (Reg. No. 38,100)
QUINN EMANUEL URQUHART &
SULLIVAN LLP

51 Madison Avenue, 22nd Floor

New York, NY 10010

Email: nickcerrito@quinnemanuel.com

Tel: (212) 849-7000

Fax: (212) 849-7100

Counsel for Patent Owner

Hangzhou DAC Biotech Co., Ltd.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing document was served in its entirety on July 19, 2023 upon the following parties via Electronic Mail:

Michael Houston
Joseph Meara
Jolene Fernandes
FOLEY & LARDNER LLP
3000 K Street, NW, Suite 600
Washington, DC 20008
682IPR@foley.com

Date: July 19, 2023

By: /s/ Nick Cerrito
F. Dominic Cerrito (Reg. No. 38,100)
QUINN EMANUEL URQUHART &
SULLIVAN LLP
51 Madison Avenue, 22nd Floor
New York, NY 10010
Email: nickcerrito@quinnemanuel.com
Tel: (212) 849-7000
Fax: (212) 849-7100

Counsel for Patent Owner
Hangzhou DAC Biotech Co., Ltd.