

U.S. Patent No. 11,767,366

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

KELONIA THERAPEUTICS, INC,
Petitioner,
v.

INTERIUS BIOTHERAPEUTICS, INC.,
Patent Owner

U.S. Patent No. 11,767,366

Case No. PGR2024-00008

**PATENT OWNER'S OPPOSITION TO PETITIONER'S
REQUEST FOR REHEARING**

TABLE OF CONTENTS

	Page
I. LEGAL STANDARD	2
II. THE BOARD DID NOT OVERLOOK EVIDENCE	2
A. The Board Was Not Required to Make an Initial Finding as to Whether a POSA Would Have Selected I182 for a Mutation	2
B. The Board Specifically Referenced the Evidence on which Petitioner Relies and Properly Rejected It	4
1. The Board Fully Considered Dr. Rose’s Declaration	4
2. The Board Did Not Err in Rejecting Unsupported Expert Testimony.....	5
3. The Testimony that Petitioner Claims the Board Overlooked Relies on Non-Prior Art Evidence and Should Not be Further Considered	10
III. THE BOARD DID NOT OVERLOOK EVIDENCE REGARDING MOTIVATION TO MAKE D OR E MUTATIONS.....	12
IV. CONCLUSION.....	14

TABLE OF AUTHORITIES

	Page(s)
Cases	
<i>Apple Inc. v. Mullen Indus. LLC</i> , No. IPR2023-00098, Paper 11 (P.T.A.B. Sept. 14, 2023).....	2, 3, 4
<i>Merck Sharp & Dohme B.V. v. Warner Chilcott Co.</i> , LLC, 711 F. App’x 633 (Fed. Cir. 2017)	8
<i>Pfizer, Inc. v. Apotex, Inc.</i> , 480 F.3d 1348 (Fed. Cir. 2007)	9, 10
<i>TQ Delta, LLC v. Cisco Sys., Inc.</i> , 942 F.3d 1352 (Fed. Cir. 2019)	10
<i>Volkswagen Grp. of Am., Inc. v. Neo Wireless LLC</i> , No. IPR2023-00426, Paper 15 (P.T.A.B. Jan. 11, 2024)	2, 4
<i>Xerox Corp. v. ByteMark, Inc.</i> , IPR2022-00624, Paper 9 (August 24, 2022)	5, 10, 14
Other Authorities	
37 C.F.R. § 42.71(d)	2, 12

Patent Owner submits this Opposition to Petitioner's Request for Rehearing at the invitation of the Patent Trial and Appeal Board via email on July 3, 2024. The Board properly denied institution, and the Request should be denied.

Contrary to Petitioner's arguments, the Board did not overlook any arguments or evidence in the Petition. Petitioner alleges that the Board failed to consider its obviousness arguments in step-wise fashion—i.e., first, narrowing the options to I182, and second, selecting which I182 mutations to make—but this was not a failure. Petitioner did not present its argument in this manner in the Petition, and the Board is not required to consider arguments that were not explicitly made.

Petitioner argues that the Board erred by overlooking testimony from its expert, Dr. Rose, regarding the selection of the claimed mutations. But the Board's decision denying institution explicitly quotes portions of expert testimony that Petitioner claims were overlooked. As explained further below, the Board correctly rejected Petitioner's arguments because it accurately found that the only support for the selection of the claimed I182E and I182D mutations was unsupported testimony from Dr. Rose.

Additionally, as explained further below, Petitioner relies heavily on the testimony of its expert, Dr. Rose, for these arguments, but Dr. Rose's testimony concerning selecting the 182nd amino acid location relies, at least in part, on

disclosures that the Board correctly found were not prior art. The Board, therefore, was entitled to disregard opinions and evidence not based on prior art disclosures.

I. LEGAL STANDARD

“The burden of showing a decision should be modified lies with the party challenging the decision. The request must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, a reply, or a sur-reply.” 37 C.F.R. § 42.71(d). When a review of the Board’s decision shows that the Board considered and understood the arguments, but simply did not find them persuasive, the request shall be denied. *See, e.g., Volkswagen Grp. of Am., Inc. v. Neo Wireless LLC*, No. IPR2023-00426, Paper 15 at 8-9 (P.T.A.B. Jan. 11, 2024); *Apple Inc. v. Mullen Indus. LLC*, No. IPR2023-00098, Paper 11 at 3 (P.T.A.B. Sept. 14, 2023).

II. THE BOARD DID NOT OVERLOOK EVIDENCE

A. The Board Was Not Required to Make an Initial Finding as to Whether a POSA Would Have Selected I182 for a Mutation

Petitioner argues that the Board abused its discretion by not separately analyzing whether a POSA would have selected the position at I182 for a mutation. Paper 12, Petitioner’s Request for Rehearing (“Req.”) at 6. As an initial matter, Petitioner fails to cite any legal support for requiring the Board to do such an analysis, and Patent Owner is not aware of any. The Board properly determined that

the claimed invention would not have been obvious to a POSA at the time of the invention in view of the asserted prior art and the evidence provided. That is all it was required to do.

Moreover, the Petition did not present its obviousness argument in the two-part manner that Petitioner now asserts the Board was required to consider. In Ground 3 of the Petition, Petitioner argues that a POSA would have been motivated to select a mutation at position 182 because the “I182 mutation is disclosed among 13 other amino acid positions for making one, two, or more mutations.” Paper 1 at 65. Petitioner then argues that a POSA would substitute aspartic acid (D) or glutamic acid (E) for isoleucine (I) at position 182. *Id.* at 66-72. Seemingly as an alternative argument, Petitioner further asserts that a “POSA would also have had a good reason to focus on *Perkins*’ express disclosure of a I182 mutation.” *Id.* at 72-74. The Petition then argues that a POSA would have allegedly arrived at an I182E mutation. *Id.* at 74-77. Thus, Petitioner’s argument did not require a two-step analysis, first assessing whether a POSA would have been motivated to select the I182 mutation and then assessing whether a POSA would have been motivated to make a I182E or I182D. The Board analyzed the arguments in precisely the same way they were presented in the Petition, and there was no legal error. *See, e.g., Apple*, No. IPR2023-00098, Paper 11 at 3 (denying request for rehearing and rejecting Petitioner’s

argument that Board overlooked a reference's inherent disclosure of a disputed claim element because "the Petition does not argue inherency").

B. The Board Specifically Referenced the Evidence on which Petitioner Relies and Properly Rejected It

Petitioner argues that the Board "overlooked Dr. Rose's testimony" regarding "whether a POSA would have selected the position of I182 out of the 13 listed positions for a making a mutation in *Perkins*." Req. at 6. While the Rehearing Request does not explicitly identify the paragraphs within the Declaration of Dr. Rose that Petitioner believes were overlooked, Petitioner seems to point to paragraphs 208-213 of the Declaration as being the relevant testimony. *See, e.g., id.* at 8-9. A review of the Board's decision denying institution, however, shows that the Board extensively considered all of the evidence, including Dr. Rose's testimony, and found it unpersuasive. *See* Paper 11 at 34-38. Accordingly, the Board should deny Petitioner's request for rehearing. *See, e.g., Volkswagen*, No. IPR2023-00426, Paper 15 at 8-9; *Apple*, No. IPR2023-00098, Paper 11 at 3.

1. The Board Fully Considered Dr. Rose's Declaration

The Board's decision denying institution discussed Dr. Rose's testimony at length. Specifically in its discussion of Ground 3, the Board extensively summarized and quoted from Dr. Rose's declaration. Paper 11 at 27-30, 35-38. In particular, the Board explicitly acknowledged Dr. Rose's testimony that it would have been obvious to a POSA to select the I182 mutation from the list of possible

mutations in Perkins as “one of the best of the 13 amino acid positions” for achieving the goal of inhibiting binding. *Id.* at 29 (citing Ex. 1002 at ¶¶ 208-210). Thus, any claim that the Board overlooked Dr. Rose’s testimony is false.

After considering the evidence of record, including Dr. Rose’s testimony, the Board found Petitioner’s arguments to be unpersuasive. In rejecting Petitioner’s arguments, the Board specifically noted that Petitioner attempted to fill in the gaps of the prior art “with reliance on RCSB PDB, Dr. Rose’s testimony (Ex. 1002 ¶¶ 195-219), and general knowledge of a person of ordinary skill in the art.” *Id.* at 36. The Board’s decision, therefore, shows that the Board did not overlook Dr. Rose’s testimony. Rather, the panel found that the evidence was unpersuasive.

2. The Board Did Not Err in Rejecting Unsupported Expert Testimony

In addition to properly considering the evidence, the Board also analyzed the evidence in the proper legal framework. Expert testimony is problematic “in cases where, like here, expert testimony is offered not simply to provide a motivation to combine prior-art teachings, but rather to supply a limitation missing from the prior art.” *Xerox Corp. v. ByteMark, Inc.*, IPR2022-00624, Paper 9 at 16 (August 24, 2022) (precedential). Petitioner relies only on Dr. Rose’s testimony for the series of steps that Petitioner claims would lead to the selection of I182 as “one of the best”

possible mutation points. Absent additional support, the Board properly found Dr. Rose's testimony to be insufficient.

Petitioner focuses on Dr. Rose testimony that a POSA would “have had good reason to focus on *Perkins*' I182 mutation from [*Perkins*] list” of possible mutations. Req. at 4. As an initial matter, Petitioner continues to distort the record—the Perkins Provisional Application discloses mutated VSV-G envelope proteins that include a mutation at one or more of many possible locations, an insertion at one or more of several locations and/or a deletion. Ex. 1006 at 17-18. Perkins does not disclose any embodiment that actually *has* a mutation at I182. Petitioner repeats its arguments that Perkins discloses “a limited list of 13 positions for making an amino acid mutation, which includes I182 as an expressly recited option.” Req. at 4. But this distorts the facts—as Dr. Rose acknowledged, every embodiment in Perkins that includes I182 as an optional mutation also includes a number of other mutations, along with insertions and deletions as options. While Dr. Rose testified that a POSA would not consider the insertions or deletions in these embodiments because “the effect of the substitutions or deletion on VSV-G protein folding are difficult to model and would require more time to investigate,” he provides no support for this assertion. Ex. 1002 at 128 n. 14. Therefore, even the starting point of Petitioner's obviousness arguments—Perkins' “limited list of 13 positions”—is artificially and improperly narrowed from the actual disclosure in Perkins.

Even accepting that Perkins disclosed a list of 13 potential mutation locations, the Board's analysis remains accurate. Petitioner relies solely on Dr. Rose's testimony to connect the dots from Perkins' broad disclosure to mutations at I182, and the Board was within its authority to discount this unsupported testimony.

Petitioner alleges that the Board improperly ignored Dr. Rose's analysis of the RCSB PDB to select I182. Req. at 7-8. For example, Petitioner argues that the Board improperly overlooked Dr. Rose's testimony that a POSA would have concluded that "I182 is one of the best of the 13 disclosed options in *Perkins* for achieving *Perkins*' express objective of inhibiting binding of VSV-G to LDL-R receptor." *Id.* at 4. While Petitioner points to Dr. Rose's explanation of the information that could be gleaned from the RCSB PDB, the Board correctly concluded that Dr. Rose did not point to any other prior art that supported the particular conclusions that he drew. For example, Dr. Rose cites to Nikolic to explain the importance of the octahedral calcium cage but does not provide any support for his assertion that a POSA would have understood that mutations at I182 would interrupt calcium binding. *See* Ex. 1002, ¶¶ 212-13; Req. at 8.

Dr. Rose's conclusions are also at odds with the disclosure of Perkins itself. Perkins cites and incorporates by reference the mutations disclosed in Nikolic. *See* Ex. 1006 at 18. As noted in Nikolic, the "atomic coordinates and structure factors have been deposited in the Protein Data Bank (accession code 5OYL and 5OY9)."

Ex. 1018 at 11. The authors of Perkins, therefore, had the same information on which Dr. Rose relies, but did not reach the same conclusions. In Perkins, I182 is one of 13 positions for a possible amino acid substitution, and is not set apart from the other possibilities in any way. Dr. Rose completely ignores the realities of Perkins' disclosure and fails to explain why the authors of Perkins did not focus on the allegedly obvious solution for achieving the stated goal of finding a mutation that "inhibits the envelope protein's ability to bind its native target, while preserving the envelope protein's fusogenic properties." Ex. 1006 at 16. Notably, Dr. Rose had the benefit of the challenged claims and the identification of I182 as the target mutation and was able to work backward and justify the steps.¹

Petitioner argues that it was legal error for the Board to decline to find Dr. Rose's testimony sufficient to establish a POSA's alleged motivation to combine the

¹ Petitioner asserts, without support, that because Dr. Rose's rationale for focusing on a I182 mutation is not expressly disclosed in the '366 patent it "cannot be labeled as mere 'hindsight' reconstruction of the claims or the inventor's path." Req. at 10. Not so. Hindsight reasoning is evidence by using the claimed invention as a "roadmap to piece together various elements" of the prior art references. *Merck Sharp & Dohme B.V. v. Warner Chilcott Co., LLC*, 711 F. App'x 633, 637 (Fed. Cir. 2017). That is exactly what Dr. Rose did here.

prior art. Req. at 7-8. Petitioner states that “such testimony is perfectly acceptable ‘to narrow the genus’ disclosed in *Perkins* to I182.” *Id.* at 5. Petitioner’s arguments, however, seem to misconstrue the Board’s decision. The Board did not fault Petitioner’s arguments for not pointing to an explicit teaching in RCSB PDB or *Perkins* for the motivation to combine. Rather, the Board noted that the testimony on which Petitioner relied was insufficient to provide “evidentiary support for a determination that the navigation of RCSB PDB crystal structures to achieve the missing limitation would have been ‘*evidently and indisputably* within the common knowledge of those skilled in the art.’” Paper 11 at 38.

Petitioner relies on *Pfizer*, but that case does not support Petitioner’s reliance on expert testimony alone. In *Pfizer*, the claimed invention was to a besylate salt of amlodipine. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1356 (Fed. Cir. 2007). The primary prior art reference disclosed “pharmaceutically-acceptable acid addition salts of amlodipine” and identified maleate as the preferred salt. *Id.* at 1353. The secondary reference disclosed 53 FDA-approved commercially marketed anions for making pharmaceutically acceptable salts, including besylate salts, from active ingredients. *Id.* at 1355. In finding the claims obvious, the Federal Circuit credited the testimony of Apotex’s expert that a POSA would have been motivated to choose an anion with a different structure than maleate. *Id.* at 1362. However, the Federal Circuit relied on a number of prior art references in finding motivation to narrow the

list of 53 anions down to a “few.” *Id.* at 1363. Here, there are no analogous references on which Petitioner can rely to narrow the options. Rather as the Board recognized, Dr. Rose’s testimony is “offered not simply to provide a motivation to combine prior-art teachings, but rather to supply a limitation missing from the prior art.” Paper 11 at 38. Therefore, the Board properly found Petitioner’s obviousness arguments based solely on the testimony of Dr. Rose unpersuasive. *Xerox Corp.*, IPR2022-00624, Paper 9 at 16 (precedential); *TQ Delta, LLC v. Cisco Sys., Inc.*, 942 F.3d 1352, 1362 (Fed. Cir. 2019) (reversing a PTAB decision finding claims obviousness because the decision relied on unsupported and conclusory expert testimony).

3. The Testimony that Petitioner Claims the Board Overlooked Relies on Non-Prior Art Evidence and Should Not be Further Considered

In addition to the Board’s findings that Dr. Rose’s testimony was unsupported, the Board’s rejection of Dr. Rose’s testimony is also proper because it was based at least in part on information that the Board properly found was not in the prior art. Specifically, Dr. Rose offered no testimony that a I182 mutation would have been obvious to a POSA in view of the *Perkins Provisional Application* (Ex. 1006) in the absence of the Perkins PCT (Ex. 1005). Instead, Dr. Rose repeatedly points to both portions of Ex. 1005 and Ex. 1006, without acknowledging the differences in their disclosures. Throughout his testimony, Dr. Rose’s testimony is tainted by the fact

that Petitioner improperly asserted that the entirety of the Perkins PCT was prior art. The Board properly determined that only the disclosure of the Perkins Provisional Application is prior art, and Petitioner has not requested rehearing on that finding. Paper 11 at 19.

Dr. Rose's opinions that an I182E mutation would have been obvious to a POSA in view of Perkins and the RCSB PDB are presented in paragraphs 188-219 of his Declaration. Throughout this testimony, Dr. Rose relies on the disclosure in the Perkins PCT of a "mutated VSV-G envelope protein compris[ing] a N180 mutation, a I182 mutation, a T352 mutation, and a E353 mutation." *See* Ex. 1002 at ¶¶ 188 (p. 116); 191; 208. This is the very sentence that the Board properly determined was not prior art. Paper 11 at 19. Therefore, there is no clear testimony from Dr. Rose that an I182E mutation would have been obvious in view of only the prior art. Dr. Rose's opinions with respect to the obviousness of a I182D mutation rely on these same paragraphs and are therefore similarly tainted. *See* Ex. 1002 at ¶ 223 (referring back to paragraphs 188-219).

Further, Petitioner complains that the Board "overlooked" Dr. Rose's testimony that "it is apparent from looking at the crystal structure of VSV-G (as deposited in *RCSB PDB*) that I182 is one of the best of the 13 disclosed options in *Perkins* for achieving *Perkins*' express objective of inhibiting binding of VSV-G to LDL-R receptor." Req. at 4, 6. For this testimony, Petitioner cites to paragraphs

208-13 of Dr. Rose's declaration. *Id.* at 4 (citing Ex. 1002 ¶¶ 208-213). Yet, paragraph 208 expressly relies on the non-prior art disclosure in the Perkins PCT of an embodiment containing mutations at N180, I182, T352, and E353. Ex. 1002 at ¶ 208. Thus, the very testimony that Petitioner claims the Board "overlooked" is based on non-prior art disclosures, and therefore, should not be further considered in the obviousness analysis. This improper reliance on disclosures not in the prior art further supports the Board's conclusions regarding Dr. Rose's testimony.

III. THE BOARD DID NOT OVERLOOK EVIDENCE REGARDING MOTIVATION TO MAKE D OR E MUTATIONS

Petitioner's Request for Rehearing includes allegations that the Board overlooked evidence regarding the reasons to select the "E" and "D" mutations for I182, but these sections do not identify with any particularity what evidence the Board allegedly overlooked and improperly raise new arguments in response to the Institution Decision. Req. at 11-14. Petitioner does not, and indeed in many instances cannot, point to where these arguments were previously raised in the petition as required by 37 C.F.R. § 42.71(d). Petitioner's arguments regarding the Board's analysis of these elements of the claims amount to nothing more than disagreement with the Board's conclusions, and should be rejected. Nevertheless, accepting Petitioner's arguments on their face, Petitioner has still failed to establish that the Board overlooked evidence.

The Institution Decision makes clear that the Board considered Dr. Rose’s testimony that it would have been obvious to a POSA to make an I182D or I182E mutation. Paper 11 at 27-29 (citing and excerpting Ex. 1002 at ¶¶ 193, 195-198, 201-204, 206); 37 (citing Ex. 1002 at ¶¶ 200, 205, 207). As explained above, the Board acknowledged that Petitioner relied on the RCSB PDB, Dr. Rose’s testimony, and knowledge of a person of ordinary skill to fill in the gaps of the prior art, but found the evidence to be unpersuasive. Paper 11 at 36.

In fact, the Board’s decision showed that the Board substantively considered the testimony. For example, the Board noted that Dr. Rose’s opinion that a “POSA would have had only two options...to oppose an interaction with negatively charged residues through anionic repulsion” was undermined by the later developed Perkins PCT expressly disclosing a I182A mutation.² Paper 11 at 36. The Board correctly found that the express disclosure of the I182A mutation

² Petitioner argues for the first time in its rehearing request that the Board “fails to appreciate that the ’366 patent also discloses a I182A mutation as its specific alternative embodiment to a I182D or I182E mutation.” Req. at 12. This argument should be rejected as waived at this stage of the proceeding—Petitioner could have asked to respond to Patent Owner’s argument in its Reply prior to institution, but chose not to.

contradicts Dr. Rose’s testimony that a POSA would have known there were “only two options” for the substitution since at least the Perkins Applicants chose a different substitution. Paper 11 at 6. The Board pointed to Patent Owner’s argument that this contradiction evidences Dr. Rose’s hindsight reasoning in developing a motivation to modify Perkins to form the claimed invention. *Id.*

Petitioner argues that “[o]nce a POSA had selected position I182...[a POSA] would have arrived at I182D or I182E through ‘common sense,’ as explained by Dr. Rose.” Req. at 13. But as the Board correctly found, the prior art does not disclose I182D or I182E mutations and the “teaching or suggestion...to create the I182E or I182D...is supplied by the bare testimony of Dr. Rose.” Paper 11 at 36. This is the precise scenario the Board flagged as problematic in *Xerox*. IPR2022-00624, Paper 9 at 16 (precedential). The Board properly declined to rely only on “common sense” to supply a limitation that is not found in the prior art. Paper 11 at 38. Thus, the Board considered the evidence related to the section of I182E and I182D substitutions and simply found the evidence to be insufficient to support institution.

IV. CONCLUSION

For at least the foregoing reasons, the Request for Rehearing should be denied.

Respectfully submitted,

Date: July 26, 2024

/Linnea Cipriano/

Linnea Cipriano (Reg. No. 67,729)

GOODWIN PROCTER LLP

620 Eighth Avenue

New York, NY 10018

lcipriano@goodwinlaw.com

Tel: +1 (212) 813-8800

Fax: +1 (212) 355-9550

Daryl Wiesen (Pro hac to be filed)

GOODWIN PROCTER LLP

100 Northern Avenue

dwiesen@goodwinlaw.com

Boston, MA 02210

Tel: +1 (617) 570-1396

Fax: +1 (617) 801-8911

Craig Lytle (Reg. No. 53,934)

GOODWIN PROCTER LLP

1900 N Street NW

Washington, DC 20036

clytle@goodwinlaw.com

Tel: +1 (202) 346-4310

Fax: +1 (202) 346-4444

Counsel for Patent owner

CERTIFICATE OF SERVICE

Pursuant to 37 CFR § 42.6(e)(4), the undersigned certifies that a true and correct copy of PATENT OWNER'S OPPOSITION TO PETITIONER'S REQUEST FOR REHEARING, was provided via email, to the Petitioner by serving the correspondence email addresses of records as follows:

naveenmodi@paulhastings.com

ericdittmann@paulhastings.com

scottpeachman@paulhastings.com

chetanbansal@paulhastings.com

Kelonia-Interius-PH@paulhastings.com

Date: July 26, 2024

/Linnea Cipriano/

Linnea Cipriano (Reg. No. 67,729)

GOODWIN PROCTER LLP

620 Eighth Avenue

New York, NY 10018

lcipriano@goodwinlaw.com

Tel: +1 (212) 813-8800

Fax: +1 (212) 355-9550

Counsel for Patent owner