

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

NOVO NORDISK A/S,

Patent Owner.

Case No. IPR2023-00722

Patent No. 8,536,122

**PETITIONER'S REPLY TO
PATENT OWNER'S PRELIMINARY RESPONSE**

TABLE OF CONTENTS

A.	Ground 3 Does Not Justify Discretionary Denial	1
B.	The Prosecution History Does Not Justify Discretionary Denial	2

TABLE OF AUTHORITIES

CASES

<i>Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH,</i> IPR2019-01469, Paper 6 (PTAB Feb. 13, 2020).....	5
<i>GMG Prods. LLC v. Traeger Pellet Grills LLC,</i> PGR2019-00024, Paper 17 (PTAB July 17, 2019)	4
<i>Hum Indus. Tech., Inc. v. Amsted Rail Co.,</i> IPR2023-00539, Paper 10 (PTAB July 26, 2023).....	5
<i>Intel Corp. v. Koninklijke Philips N.V.,</i> IPR2021-00370, Paper 10 (PTAB July 6, 2021).....	4
<i>ShenZhen Apaltek Co. v. Asetek Danmark A/S,</i> IPR2022-01317, Paper 7 (PTAB Feb. 6, 2023).....	3
<i>Teradata Corp. v. SAP SE,</i> IPR2020-00943, Paper 12 (PTAB Nov. 25, 2020).....	3
<i>Thorne Rsch., Inc. v. Trs. of Dartmouth Coll.,</i> IPR2021-00491, Paper 18 (PTAB Aug. 12, 2021).....	3

OTHER AUTHORITIES

37 C.F.R. § 42.23(b)	2
MPEP 2131.02(I)	3
MPEP 2144.08	3

With the Board’s authorization, Petitioner submits this Reply to address two bases Patent Owner alleges justify denial of institution. Neither basis has merit.

A. Ground 3 does not justify discretionary denial

Patent Owner, citing the *title* of Ground 3, complains of “extraordinary vagueness” and insists with a straight face that it lacks “any meaningful opportunity ... to respond.” POPR 19. But Patent Owner *does* respond on the merits to Ground 3. *See* POPR 52-57. Ground 3 relies on the same prior art as Grounds 1 and 2, and provides specific prior-art and declaration citations for (1) the prior-art disclosures of the structural fragments of semaglutide and their properties and (2) a POSA’s motivation to combine those disclosures. The only difference is the analytical framework for a POSA’s motivation: while Grounds 1 and 2 apply the narrower lead-compound analysis, Ground 3 explains that a POSA would have been motivated to reach semaglutide from the same prior art applying broader obviousness principles—routine optimization of known result-effective variables—because that is how drug discovery worked at the priority date.

In particular, Ground 3 explains that the three requisite modifications to liraglutide involved sites known to affect bioactivity in specific ways, that there was a limited range of realistic options, and that screening those options would have been a routine part of drug discovery. Pet. 62-65. Ground 3 explained with particularity (1) why the Aib⁸ modification would have been obvious, Pet. 62-63; (2) why the

fatty diacid modification would have been obvious, Pet. 62-63; and (3) why the di-AEEA spacer modification would have been obvious, Pet. 62, 64. Although Patent Owner insists that the number of options was large and unpredictable, those are issues of fact for expert testimony and trial. Ground 3 also relies on the same prior art for each claim limitation as Grounds 1 and 2. *See* Pet. 19-26. The additional references Patent Owner complains of give context to show a POSA's skill level and background knowledge; they confirm the declarations are well-reasoned and the references are not used to show disclosures of the limitations. And although Patent Owner complains Petitioner is "empower[ed]" by Ground 3 "to argue whatever it wants throughout the remainder of this proceeding," that is hyperbole. The rules ensure Petitioner keeps to the Petition's framing. 37 C.F.R. § 42.23(b).

Patent Owner also insists Ground 3 merits denying the whole Petition. POPR 19. But its cases do not support such a draconian request. In *Adaptics*, *EnergySource*, *InVue*, *ADT*, *John Crane*, and *Sainty Sumex*, every obviousness ground was deficient in some way, and many involved a complete failure to explain, or they asserted legally impossible arguments like multi-reference anticipation. Nor is Ground 3 a "catch-all" like in many of those cases—it is a different motivation theory.

B. The prosecution history does not justify discretionary denial

Even if some art appeared in the prosecution of the '122 patent (or its '343

parent), as Patent Owner contends, that does not warrant discretionary denial because the Petition presents a new combination of art and a new analytical framework never considered by the Examiner during prosecution. During the '343 prosecution, the Examiner evaluated the obviousness of the claims—directed first to a subgenus of GLP-1 inhibitors, then a narrower example—in view of the Knudsen Patent, which taught a broad genus of GLP-1 analogues and classes of possible modifications, consistent with MPEP 2144.08 (describing obviousness of species/subgenus over genus). The Petition, however, takes an entirely different approach by identifying a single compound (liraglutide) and proposing specific modifications to arrive at an obvious species that falls within the scope of the claims, consistent with MPEP 2131.02(I). The Petition is therefore not repetitive of what happened during prosecution, and the Board should not invoke its discretion.

Advanced Bionics part one (same art/argument). For the “same art” prong, the inquiry focuses on whether the totality of the art in the Petition overlaps with that cited during prosecution, not only whether individual references appear in both. *See, e.g., ShenZhen Apaltek Co. v. Asetek Danmark A/S*, IPR2022-01317, Paper 7, 9 (PTAB Feb. 6, 2023) (use of same reference does not constitute “same art” when part of “a significantly different combination than was previously considered by the Examiner”); *see also Thorne Rsch., Inc. v. Trs. of Dartmouth Coll.*, IPR2021-00491, Paper 18, 8-9 (PTAB Aug. 12, 2021); *Teradata Corp. v. SAP SE*, IPR2020-00943,

Paper 12, 23-24 (PTAB Nov. 25, 2020). Although the Examiner cited the Knudsen Patent in the '343 prosecution as teaching a genus of GLP-1 analogues and possible further modifications generally, the Examiner never considered any of the art combinations proposed in the Petition (e.g., combining Knudsen 2004 or 2001 with the Knudsen Patent, Bridon, and Dong). Indeed, after the applicant narrowed the claims from a subgenus to the compound of Example 4, Ex. 1004, 34, the Examiner allowed the claims without identifying any of the art that taught the specific GLP-1 backbone, spacer, and sidechain, *id.* at 26-27, in contrast to the Petition here.

Patent Owner incorrectly contends Knudsen 2001 and 2004 are cumulative of the Knudsen Patent. POPR 62-63. But “[b]y merely quoting references without comparing them to [the references before the Patent Office], Patent Owner oversimplifies the analysis.” *Intel Corp. v. Koninklijke Philips N.V.*, IPR2021-00370, Paper 10, 8 (PTAB July 6, 2021). Of the possible GLP-1 analogues, Knudsen 2001 and 2004 both identify liraglutide as advancing through clinical trials, Ex. 1010, 3; Ex. 1011, 5—a significant reason to select it as a lead. The Knudsen Patent, while *supporting* that selection, describes liraglutide as one of over 75 example analogues. Ex. 1012, 174:9-216:14. As for Bridon, even if certain of its teachings overlap to some extent to art cited on the face of the '122 patent, a reference cited but not previously applied should be given little weight. *See GMG Prods. LLC v. Traeger Pellet Grills LLC*, PGR2019-00024, Paper 17, 27 (PTAB July 17, 2019).

For the “new argument” prong, Patent Owner contends without support that the Petition “lay[s] out substantially the same path” as the Examiner, but concedes a lead-compound analysis was never performed. POPR 65-66. This is a new argument. Further, Patent Owner points to no factual finding by the Examiner that this Petition asks the Office to reconsider. Thus, Patent Owner fails at step one.

Advanced Bionics part two (material error). Even if the Board were to reach step two, institution is still favored if the Petition demonstrates a reasonable likelihood of unpatentability over references that appeared in the file history, but the Examiner failed to apply in combination. *Hum Indus. Tech., Inc. v. Amsted Rail Co.*, IPR2023-00539, Paper 10, 51-53 (PTAB July 26, 2023). “[M]aterial error may include misapprehending or overlooking specific teachings of the relevant prior art.” *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6, 8 n.9 (PTAB Feb. 13, 2020). Here, the Examiner materially erred by failing to identify liraglutide and the *specific* modifications that could be made to it within the prior art before them, to arrive at an obvious species that would fall within the scope of the claims. The Examiner further erred by failing to apply a lead-compound analysis (or something like it, as in Ground 3), and instead simply performed a genus-to-subgenus obviousness analysis. Moreover, the Examiner identified no reference as teaching the di-AEEA spacer.

Respectfully submitted,
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Dated: August 10, 2023

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CERTIFICATE OF SERVICE

I certify that I caused to be served the foregoing **PETITIONER'S REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE** electronically by email on **August 10, 2023** in their entirety on the following counsel of record for Patent Owner:

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