

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CSPC MEGALITH BIOPHARMACEUTICAL CO., LTD.,

Petitioner,

v.

SHANGHAI MIRACOGEN INC.,

Patent Owner.

Case No. IPR2025-00685

U.S. Patent No. 10,792,370

**PATENT OWNER'S REQUEST FOR
DISCRETIONARY DENIAL OF INSTITUTION**

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PATENT OWNER'S EXHIBIT LIST

Exhibit No.	Description
2001	International Nonproprietary Names for Pharmaceutical Substances, WHO Drug Information, Vol. 38, No. 2, 2024
2002	Fei Han et al., Becotatug vedotin vs. chemotherapy in pre-heavily treated advanced nasopharyngeal carcinoma: A randomized, controlled, multicenter, open-label study
2003	Lepu Biopharma Co., Ltd., Voluntary Announcement, Breakthrough Therapy Designation Granted by the FDA to MRG003 for the Treatment of R/M NPC
2004	U.S. Food & Drug Administration, Fast Track
2005	U.S. Food & Drug Administration, Breakthrough Therapy

I. Introduction

The Petition presents a replay of what the Office has already seen and addressed during examination of the '370 patent. Petitioner structures the grounds in the same way as the Examiner structured section 103 rejections, using references either explicitly considered during prosecution or with teachings essentially cumulative to considered art. Petitioner does not present any meaningful new facts or evidence, nor does it identify a genuine error, that would warrant a second look from the Board. The Director should deny institution and avoid wasting the Board's resources on arguments and art that have already been thoroughly considered and overcome.

Furthermore, compelling public health interest weighs in favor of denying institution because the '370 patent is related to Patent Owner's MRG003 drug candidate that has been granted Fast Track and Breakthrough Therapy designations by the Food and Drug Administration.

II. Institution Should Be Denied Under 35 U.S.C. § 325(d) and *Advanced Bionics*.

The Director should exercise discretion under 35 U.S.C. § 325(d) to deny institution of inter partes review because the Petition's grounds present substantially the same art and arguments considered by the Examiner during prosecution of the '370 patent. Petitioner cannot demonstrate error by the

Examiner because its grounds suffer from the same deficiencies as the rejections in Office Actions.

Section 325(d) provides that the Director may elect to not institute a proceeding if the challenge to the patent is based on matters previously presented to the Office. *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GMBH*, IPR2019-01469, Paper 6 at 10 (PTAB Feb. 13, 2020) (precedential).

Section 325(d) states, in pertinent part, “[i]n determining whether to institute or order a proceeding . . . , the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.”

Under section 325(d), the Director uses a two-part analysis, considering: (1) whether the same or substantially the same art or arguments were presented to the Office during original prosecution; and (2) whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics, Paper 6 at 10. For part (1), the Director considers *Becton* factors (a), (b), and (d):

(a) the similarities and material differences between the asserted art and the prior art involved during examination;

(b) the cumulative nature of the asserted art and the prior art evaluated during examination; and

(d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art.

Id.; *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17-18 (PTAB Dec. 15, 2017) (precedential). For part (2), the Director considers Becton factors (c), (e), and (f):

(c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;

(e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and

(f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Id.

A. Petitioner’s art and arguments are substantially the same as those considered by the Examiner.

Two of Petitioner’s three references, Liu and Leanna, were considered by the Examiner. The only new reference is Wei, but the Petitioner’s own statements demonstrate that its relied-upon teachings are not materially different from those of Leanna. Furthermore, Petitioner uses the references for substantially the same teachings and arguments as the Examiner did during prosecution, essentially asking the Board to repeat the Examiner’s work.

1. The Liu and Leanna references were considered during prosecution.

The Petition includes two grounds: a combination of Wei and Liu, and a combination of Leanna, Liu, and Wei. Leanna and Liu were included on an Information Disclosure Statement filed with the original patent application. Ex-1003, 102. The Examiner certified that the IDS had been considered. Ex-1004, 101-02. The Examiner even used Liu as a basis of rejections in all three Office Actions, and noted that Liu is “CN103772504 reference of the IDS filed 8/14/2017.” Ex-1003, 402. There can be no dispute that the Examiner carefully considered Liu and Leanna.

Petitioner appears to suggest that Leanna was overlooked by the Examiner, stating that Leanna “w[as] never discussed by the Office or the Applicant during prosecution.” Pet. 34. But there can be no doubt that the Examiner considered the reference because it was the only other reference on the IDS that included Liu, the Examiner’s rejection based on Liu noted that Liu came from the IDS, and the Examiner certified she considered the references on the IDS. In *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 2-4 (PTAB May 19, 2025) (precedential), the Director found a reference was presented to the Office even though it was cited in an IDS containing over 1,000 references. Here, the IDS lists only 2 references and Petitioner cannot reasonably argue that the Examiner somehow did not consider Leanna.

2. Petitioner implicitly admits that the relied-upon teachings of the new reference, Wei, are cumulative of Leanna.

Petitioner focuses on alleging that Wei and Leanna are different from Tikhomirov, the primary reference used in Office Actions, but in doing so demonstrates that the relied-upon teachings of Wei are substantially similar to Leanna. Pet. 34. For various aspects of Wei and Leanna’s teachings used in the Petition, Petitioner contends that they are the same:

- “Wei and Leanna disclose anti-EGFR ADCs with cleavable linkers without any toxicity concerns associated with cleavable linkers;”
- “Wei and Leanna do not focus exclusively on non-cleavable linkers but have working examples of ADCs using cleavable linkers;”
- Wei and Leanna “extensively discuss and teach ADCs with cleavable linkers, including the specific vc cleavable linker disclosed as a preferred embodiment and claimed in the ’370 patent;”
- “[S]ubstantial amounts of the experimental data in Wei and Leanna are directed to anti-EGFR ADCs using cleavable linkers;”
- “[N]othing in Wei and Leanna would indicate to a POSA that cleavable linkers used in anti-EGFR ADCs are disfavored;”
- “Wei and Leanna teach that a ‘safe anti-EGFR ADC’ can incorporate a strongly antagonistic anti-EGFR antibody linked to an

antimicrotubule payload by a cleavable linker, especially since these references have disclosures and claims of pharmaceutical compositions and methods of treatment using these cleavable linker ADCs.”

Pet. 34, 44-45.

A comparison between Ground 1 and Ground 2 further shows that Petitioner uses Wei for substantially the same teachings as those of Leanna. Pet. 37-38, 65-66. For example, Petitioner uses essentially the same language to describe the relevant disclosures of Wei and Leanna:

Wei	“An anti-EGFR antibody-drug conjugate ..., that comprises an anti-EGFR antibody ... covalently linked to a cytotoxic agent MMAE via a cleavable valine-citrulline (vc) linker.”
Leanna	“An anti-EGFR antibody-drug conjugate, ... that comprises a humanized anti-EGFR antibody ... covalently linked to a cytotoxic agent MMAE via a cleavable valine-citrulline (vc) linker.”

Compare Pet., 37-38 *with* Pet., 65-66. The purported difference between Wei and Leanna, according to Petitioner, appears to be the specific humanized anti-EGFR antibody used. Pet. 68. This purported difference is immaterial because both Wei and Leanna teach humanized antibodies and their antibodies are replaced with that of Liu according to the grounds.

Because Leanna was considered during prosecution and Petitioner relies on Wei's teachings that are cumulative of Leanna, the Petition includes substantially the same art that was presented to the Office during original prosecution. *Becton* factors (a) and (b) favor denial of institution.

3. Petitioner uses Wei and Leanna for substantially the same teachings and arguments as the Examiner used Tikhomirov for during prosecution.

During prosecution, the rejections were based on combinations of Tikhomirov, Liu, and other references. The Petition's grounds propose to replace Tikhomirov with Wei or Leanna. But a closer examination shows that the teachings of Wei and Leanna, as relied on in the Petition, are substantially the same as what the Examiner relied on Tikhomirov for. During prosecution, the Examiner cited Tikhomirov's teachings of an "EGFR antibody in a form conjugated with an anti-microtubule toxin," including an embodiment with "conjugation of cetuximab to MMAE anti-microtubule payload by a cleavable linker." Ex-1004, 153-54, 244. The Examiner cited Liu for its teaching of the BA03 antibody and argued that "[i]t would have been prima facie obvious as of the effective filing date to use the BA03 antibody in place of cetuximab in the conjugates and methods of using the conjugates of Tikhomirov." Ex-1004, 156, 247.

For Ground 1, Petitioner relies on Wei for its disclosure of an anti-EGFR antibody (“a modified cetuximab antibody”) conjugated with MMAE “via a cleavable valine-citrulline (vc) linker.” Pet. 38. This is the same as what the Examiner cited Tikhomirov as teaching. Petitioner argues that “Liu discloses and claims the humanized version of cetuximab—BA03—and states that BA03 has numerous benefits over cetuximab.” Pet. 40, 67. Petitioner argues that a POSA would have been motivated to replace Wei’s antibody with the humanized cetuximab antibody of Liu. Pet. 40-42. This recycles the Examiner’s rationale for combining Tikhomirov and Liu.

Similarly, for Ground 2, Petitioner argues that Leanna discloses “[a]n anti-EGFR antibody-drug conjugate ... that comprises a humanized anti-EGFR antibody ... covalently linked to a cytotoxic agent MMAE via a cleavable valine-citrulline (vc) linker.” Pet. 65-66. Relying on the same teaching of Liu, Petitioner argues that a POSA would have been motivated to replace Leanna’s antibody with that of Liu. Pet. 67-69.¹ This again uses Leanna and Liu in the same manner and for substantially the same teachings as the Examiner used Tikhomirov and Liu.

¹ For Ground 2, Petitioner contends that Leanna and Liu teach all the limitations of claim 1, while Wei provides additional motivations to combine Leanna and Liu. Pet. 65-69.

Indeed, in alleging that its reasoning to combine Wei/Leanna with Liu was not challenged during prosecution, Petitioner admits that it combines Wei/Leanna with Liu in the same way as the Examiner combined Tikhomirov with Liu. Pet. 42 (“This reasoning—that the POSA would be motivated to replace cetuximab in prior-art ADC references with the humanized cetuximab antibody of Liu—was never even challenged, let alone overcome, by the Patent Owner during prosecution.”), 69 (“This reasoning—that the POSA would be motivated to replace cetuximab in prior-art ADC references with the humanized cetuximab antibody of Liu—was never challenged by Patent Owner during prosecution.”).

Petitioner’s attempt to show differences between the grounds in the Petition and the Office Actions is unavailing. Petitioner seeks to distinguish Wei and Leanna from Tikhomirov based on its assertions that (1) Wei and Leanna focus more on cleavable linkers, (2) Wei and Leanna include “substantial amounts of experimental data” directed to cleavable linkers, and (3) Wei and Leanna do not indicate cleavable linkers are disfavored. Pet. 44-45.

However, as explained above, Petitioner relies on Wei/Leanna for substantially the same teachings as what the Examiner relied on Tikhomirov for and admittedly combines Wei/Leanna with Liu in the same manner as the Examiner combined Tikhomirov with Liu. Petitioner’s characterization of the references’ “focus” is unrelated to the question whether their teachings are

substantially different. What matters is that Petitioner fails to point to teachings available in Wei/Leanna that are not available in Tikhomirov.

Petitioner's purported "substantial amounts of experimental data" directed to cleavable linkers in Wei and Leanna, even if true, do not make the Petition's grounds substantially different from what the Examiner considered. This is because the Examiner did consider Leanna in examining the '370 patent. Having considered Leanna and other references, the Examiner cited Polson as teaching "antibody drug conjugates with cleavable linkers have broad efficacy and are relatively insensitive to target biology compare to ADCs with a non-cleavable ... linker." Ex-1004, 160. The Examiner further combined Tikhomirov and Liu with Doronina to support a motivation to use a cleavable linker, where Doronina was cited for teaching "[a] conjugate with the cleavable linker has a potency of over 270X that of [a] conjugate with the non-cleavable linkers" and argued that "[o]ne of skill in the art would have been motivated to [use a cleavable linker] by the teachings of Doronina et al. ..." Ex-1004, 247-48. Because the Examiner always had Leanna's data in her possession and used experimental data directed to cleavable linkers in her Office Actions, purported experimental data from Wei and Leanna do not make the Petition's grounds materially different.

Petitioner's argument that Wei and Leanna do not indicate cleavable linkers are disfavored is similarly unavailing. In the last Office Action response, the

Applicant pointed out that Tikhomirov disclosed that “Figure 13 shows that conjugation of cetuximab to MMAE by a cleavable linker (valine-citrulline) potentiates its toxicity against normal cells and MDA-MB-468 cancer cells, whereas conjugation via non-cleavable linker (SMCC) potentiates anti-cancer activity” and stated that “a safe anti-EGFR ADC should incorporate a strongly antagonistic anti-EGFR antibody linked to an anti-microtubule payload by a non-cleavable linker.” Ex-1004, 299-300. The Applicant argued that “in view of the disclosure of [Tikhomirov], one of ordinary skill in the art would be discouraged from using a cleavable linker in incorporating a strongly antagonistic anti-EGFR antibody into an ADC due to potentiated toxicity against normal cells of such ADCs.” Ex-1004, 300.

Each of Petitioner’s grounds requires replacing the antibody of Wei/Leanna with that of Liu. Pet. 42, 69. In other words, the Examiner’s combination of Tikhomirov and Liu, Petitioner’s combination of Wei and Liu, and Petitioner’s combination of Leanna, Liu, and Wei all use the same antibody of Liu. Given that Liu’s antibody is a strongly antagonistic anti-EGFR antibody, Tikhomirov’s statement that “a safe anti-EGFR ADC should incorporate a strongly antagonistic anti-EGFR antibody linked to an anti-microtubule payload by a non-cleavable linker” and the Applicant’s related arguments are equally applicable to the Petitioner’s grounds. Here, a POSA is presumed to know Tikhomirov, including its

explanations regarding toxicity. *Custom Accessories, Inc. v. Jeffrey–Allan Indust., Inc.*, 807 F.2d 955, 962 (Fed.Cir.1986) (“The person of ordinary skill ... is presumed to be aware of all the pertinent prior art.”). Merely excluding Tikhomirov from the obviousness combinations does not remove its teachings from a POSA’s knowledge or make the Petition’s grounds materially different from what the Examiner considered.

Because the manner in which Petitioner relies on the prior art is substantially the same as the arguments made during examination, *Becton* factor (d) favors denial of institution.

B. Petitioner fails to show that the Office erred during prosecution.

The Petition alleges material error by the Office, claiming that “[t]he Office was misled in allowing the claims based on Patent Owner’s defective ‘teaching away’ and unexpected results arguments.” Pet. 45-51. Instead of pointing to any error in the Examiner’s statements in the record, Petitioner criticizes the Applicant’s arguments during prosecution. According to *Advanced Bionics*, “[a]n example of a material error may include misapprehending or overlooking specific teachings of the relevant prior art where those teachings impact patentability of the challenged claims” and “[a]nother example may include an error of law, such as misconstruing a claim term, where the construction impacts patentability of the challenged claims.” *Advanced Bionics*, Paper 6 at 8-9 n.9. Here, the Examiner

issued two Office Actions addressing the Applicant's arguments before issuing the Notice of Allowance. Ex-1004, 146-62, 240-52. Petitioner does not identify any misapprehension/oversight or error of law shown by the Examiner's statements in the record. As further explained below, Petitioner fails to show error in the Examiner's allowance of the '370 patent.

1. Petitioner fails to show error in the Examiner's consideration of the argument that a POSA would not have been motivated to combine Tikhomirov with Liu.

In the response to Office Action dated March 26, 2020, the Applicant argued that "one skilled in the art would not have been motivated ... to use a cleavable linker to arrive at the ADC ... as claimed." Ex-1004, 299. The Applicant pointed out that "Figure 13 [of Tikhomirov] shows that conjugation of cetuximab to MMAE by a cleavable linker (valine-citrulline) potentiates its toxicity against normal cells and MDA-MB-468 cancer cells, whereas conjugation via non-cleavable linker (SMCC) potentiates anti-cancer activity." *Id.* Based on Tikhomirov's discussion of its Figure 13, the Applicant argued that "one of ordinary skill in the art would be discouraged from using a cleavable linker in incorporating a strongly antagonistic anti-EGFR antibody into an ADC due to potentiated toxicity against normal cells of such ADCs." Ex-1004, 299-300. The Examiner issued a Notice of Allowance thereafter. Ex-1004, 306-313.

Rather than addressing the Examiner's analysis and reasoning, Petitioner's allegation of error focuses on attacking the credibility of Tikhomirov's teachings and experimental results based on conclusory and uncorroborated expert testimony. Pet. 45 ("Dr. Bournazos points out many serious errors within Figure 13 [of Tikhomirov]."). This is fundamentally a criticism of the prior art, rather than an error by the Office.

Furthermore, Petitioner's expert testimony misunderstands Tikhomirov. Dr. Bournazos argues that Tikhomirov's disclosure is "highly suspect" because it does not contain a "head-to-head comparison" or a "statistical comparison" and there was "a single observation." Pet. 45-46; Ex-1002, ¶¶102-104. This argument, however, misses an important point that the data in Figure 13 of Tikhomirov was not directed to comparing ADCs with DM1 and MMAE per se, but was directed to understanding how differently the ADCs performed against tumor cells and non-tumor keratinocytes. Ex-1009, 9-10, 29-30, Fig. 13. Against tumor cells, where the linkers were assumed to have limited impacts, both types of ADCs had similar cytotoxicity. *Id.* Against non-tumor cells, however, the ADCs with the cleavable linker (Cetux 2C9-MMAE) exhibited significantly higher toxicity than the ones with the non-cleavable linkers, which the POSA would have readily appreciated to be attributed to the cleavable linker. *Id.* To the extent Dr. Bournazos asserts that the comparison in Figure 13 is not statistical, this assertion is misplaced. As seen

in the figure, each curve is presented with error bars. Ex-1009, Fig. 13. The short error bars for each relevant curve, in view of the large distances between the curves, are clearly indicative of statistical significance. Petitioner further argues that Tikhomirov's observation "only applies to anti-microtubule payloads." Pet. 47; Ex-1002, ¶105. However, Petitioner cannot reasonably argue that Tikhomirov's observation does not apply to its grounds because both grounds involve ADCs with the anti-microtubule payload MMAE.

Even if Dr. Bournazos's testimony is determined to have merit, it at most shows that Tikhomirov does not definitively prove that cleavable linkers always potentiate toxicity against normal cells when used in ADCs with strongly antagonistic antibodies. However, definitive proof is not required for a reference to teach away from or cast doubt on a combination. *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994) ("A reference may be said to teach away when a person of ordinary skill, upon [examining] 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."). Furthermore, "[e]ven if evidence does not 'rise to the level of teaching away,' it is still proper for the Board to consider evidence that 'suggests reasons that a skilled artisan would be discouraged from pursuing such a combination.'" *Laboratory Corp. of Am. Holdings v. Ravgen, Inc.*, No. 2023-1342, 2025 WL 32904, at *4 (Fed. Cir. Jan. 6,

2025) (non-precedential) (citing *Arctic Cat Inc. v. Bombardier Recreational Prods. Inc.*, 876 F.3d 1350, 1363 (Fed. Cir. 2017)).

Dr. Bournazos's testimony at most challenges the strength of Tikhomirov's disclosure, but in no way rebut that Tikhomirov's discussion of experimental data and its statement that "a safe anti-EGFR ADC should incorporate a strongly antagonistic anti-EGFR antibody linked to an anti-microtubule payload by a non-cleavable linker" would have led or suggested a POSA to use a non-cleavable rather than cleavable linker.

The *Advanced Bionics* framework "reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown," where "[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*, Paper 6 at 9. Dr. Bournazos's attack on the strength of Tikhomirov's disclosure does not even come close to showing that a reasonable mind cannot find Tikhomirov to discourage a POSA from using cleavable linkers with Liu's strongly antagonistic antibody.

2. Petitioner fails to show the Petition's grounds do not suffer from the deficiencies of the art considered by the Examiner.

Petitioner does not explain how the deficiencies of the Tikhomirov-Liu combination that resulted in allowance of the '370 patent do not also apply to the Petition's grounds. As explained above, Petitioner's argument that a POSA would

have been discouraged from using a cleavable linker in incorporating a strongly antagonistic anti-EGFR antibody into an ADC due to potentiated toxicity against normal cells led to allowance of the '370 patent. *Supra* §II.B.1.

In the section discussing motivation to combine Wei with Liu, Petitioner does not demonstrate why replacing Wei's antibody with Liu's antibody would have resulted in an ADC with an acceptable toxicity. *See* Pet. 40-42. Petitioner admits that Wei's particular humanized version of cetuximab variant, huY104D, "exhibited reduced growth inhibition of non-tumor cells" due to its pH selectivity. Pet. 41. However, Petitioner does not contend that Liu's antibody has a similar characteristic and does not explain why replacing Wei's antibody with Liu's would not have materially increased the toxicity. Similarly for the combination of Leanna, Liu, and Wei, Petitioner does not explain whether the combination would have resulted in an ADC with acceptable toxicity. Pet. 67-69.

Petitioner's only arguments on the toxicity issue are (1) Wei and Leanna disclose anti-EGFR ADCs with cleavable linkers without toxicity concerns and (2) cleavable linkers have been used in FDA approved ADCs, including those approved after the filing of the '370 patent. Pet. 2-3, 34, 50, 67. However, neither the properties of unmodified ADCs of Wei and Leanna nor that of unrelated drugs approved by the FDA answer the question whether replacing Wei/Leanna's antibody with Liu's strongly antagonistic antibody would have resulted in

acceptable toxicity. Petitioner cannot show error of the Office when its own grounds suffer from the same deficiencies as what the Examiner considered.

3. Petitioner fails to show error in the Examiner's consideration of the unexpected results argument.

Petitioner argues that the Office was misled in allowing the claims based on Patent Owner's unexpected results argument. Pet. 45. However, Petitioner fails to show the Examiner relied on the Applicant's unexpected results argument as a basis for allowing the '370 patent.

The Applicant raised an unexpected results argument in the July 1, 2019 and December 16, 2019 responses to Office Action (Ex-1004, 139-40, 203-04), but did not raise this argument in the March 26, 2020 response to Office Action (Ex-1004, 298-302), after which the Notice of Allowance was issued. In the Applicant's last response to Office Action, the Applicant recounted arguments in the preceding Office Action responses and noted that the Examiner's rejection had changed with a newly cited reference Doronina. Ex-1004, 298. In response to the new rejection, Applicant focused on motivation to combine and argued that "one skilled in the art would not have been motivated by the cited references, including newly cited [Doronina reference], to use a cleavable linker to arrive at the ADC or a pharmaceutically acceptable salt thereof as claimed in the present application." Ex-1004, 299-300. The Applicant did not raise the unexpected results argument in this response. Ex-1004, 298-302.

Petitioner does not address the fact that Applicant's unexpected results argument was not presented in the Office Action response preceding the Notice of Allowance and, thus, fails to show that this argument was the basis for allowance. Without this showing, Petitioner cannot establish material error committed by the Office in relation to the unexpected results argument.

As shown above, *Becton* factors (c) weighs in favor of denying institution because the Examiner used Tikhomirov as the primary reference in Office Actions and relied on Tikhomirov's teachings that are substantially the same as what Petitioner now relies on from Wei and Leanna. The Petitioner fails to show error by the Examiner in her evaluation of prior art, let alone establishing that any error is material to patentability (Factor (e)). Finally, any additional evidence and facts presented in the Petition do not warrant reconsideration of the prior art or arguments because they do not show how the deficiencies of the art considered by the Examiner do not apply to the Petition's grounds (Factor (f)).

III. Institution Should Be Denied Based on Other Factors of Discretionary Denial

The Acting Director's March 26, 2025 Memorandum regarding Interim Processes for PTAB Workload Management (the "Memo") provides a list of factors related to discretionary denial, including "[w]hether there have been changes in the law or new judicial precedent issued since issuance of the claims that may affect patentability," "[t]he strength of the unpatentability challenge," and

“[c]ompelling economic, public health, or national security interests.” Memo at 2. These factors weigh in favor of discretionary denial of the Petition.

A. The unpatentability challenge is weak on the merits and should be denied.

In accordance with the Office’s “FAQs for Interim Processes for PTAB Workload Management,” Patent Owner directs attention to, and incorporates by reference, the forthcoming Patent Owner’s Preliminary Response. *See* FAQ 25. As will be apparent from the POPR, the weak merit of the grounds warrants discretionary denial of the Petition.

B. Institution should be denied in light of compelling public health interest.

The ’370 patent is directed to Patent Owner’s drug candidate MRG003 (an EGFR-targeted ADC, becotatug vedotin). Ex-2001, 000028-30; Ex-2002, 000001. MRG003 has been granted Fast Track designation and Breakthrough Therapy designation by FDA for the treatment of recurrent or metastatic nasopharyngeal cancer (“R/M NPC”). Ex-2003, 000001.

Fast Track “is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need,” with a purpose of “get[ting] important new drugs to the patient earlier.” Ex-2004, 000001. “Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially better than available

therapy.” *Id.* “Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).” Ex-2005, 000001.

The FDA’s Fast Track and Breakthrough Therapy designations demonstrate the compelling public health interest in making the drug corresponding to MRG003 available to patients with serious R/M NPC in an expeditious manner. The urgency and importance of the drug is confirmed by the FDA’s determination that the therapy corresponding to MRG003 currently does not exist or may demonstrate substantial improvement over available therapy.

Not only would an IPR waste resources of the Board and the parties by re-litigating issues that the Examiner has considered, it would also create uncertainties on the Patent Owner’s ability to commercialize the MRG003 drug candidate. This would inevitably delay the process of making this therapy available to patients who are desperately in need of treatment. Therefore, compelling public health interest weighs in favor of denying institution.

C. There have not been changes in the law or new judicial precedent issued since issuance of the claims that may affect patentability.

The ’370 patent was issued October 6, 2020. Patent Owner is not aware of changes in the law or new judicial precedent that would affect patentability of the

'370 patent. The Petition does not allege that the Examiner made an error of law or that the law has changed. This factor favors discretionary denial because no change in the law warrants the Board to expense time and resources to repeat the analysis that has been done by the Examiner.

IV. Conclusion

For the foregoing reasons, the Director should exercise discretion to deny institution under 35 U.S.C. § 325(d) and *Advanced Bionics*, as well as in light of other factors in favor of discretionary denial.

Date: June 6, 2025

Respectfully,

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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that the foregoing Patent Owner’s Request for Discretionary Denial of Institution contains 4,667 words and therefore complies with the 14,000-word type-volume limit specified by the Memo. The word count does not include those portions excepted by 37 C.F.R. §42.24(c) and was calculated by Microsoft Word 365.

Date: June 6, 2025

By: */Christopher Ponder/*
Christopher Ponder

CERTIFICATE OF SERVICE

The undersigned hereby certifies that, on this date, a complete copy of the foregoing Patent Owner's Request for Discretionary Denial of Institution was served via email to all parties to this proceeding at the addresses indicated:

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