

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BPI LABS, LLC,
PETITIONER,

v.

ELI LILLY AND COMPANY
PATENT OWNER.

Case IPR2025-01346
Patent 9,474,780

**PETITIONER BPI LABS, LLC'S OPPOSITION TO PATENT OWNER'S
BRIEF ON DISCRETIONARY DENIAL**

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LIST OF EXHIBITS¹

Exhibit No	Description
1001	U.S. Patent No. 9,474,780.
1002	Declaration of Virginia Cornish, PH.D. in support of IPR2025-01024.
1003	<i>Intentionally left blank.</i>
1004	Prosecution History (Excerpts) of U.S. Patent No. 9,474,780.
1005	WO 2016/111971 Search Report.
1006	WO 2016/111971 Written Opinion.
1007	WO 2011/119657 A1 Publication (Alsina-Fernandez).
1008	WO 2013/164483 A1 Publication (Just).
1009	WO 2006/097537 A2 Publication (Lau)
1010	WO 2014/202727 A1 Publication.
1011	Fields G. B. Introduction to peptide synthesis. <i>Current protocols in protein science, Chapter 18</i> , 2002; 18.1.1–18.1.9.
1012	US 2015/0299281 A1 Publication.
1013	SAXENDA (liraglutide) injection drug label (Dec. 2014) (“SAXENDA”) available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/206321Orig1s000lbl.pdf .
1014	Nelson, D. L., <i>et al.</i> , Chapters 4-5, 7, <i>Lehninger Principles of Biochemistry</i> , 3rd ed. (eds. Ryan, M., <i>et al.</i> , Worth Publishers) 2000.
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1017	WO 2011/119657 A1 Publication (Alsina-Fernandez).

¹ For ease of reference Petitioner uses the same exhibit numbering scheme as used in IPR2025-01024 for the same exhibits.

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1084	Declaration of Dr. Zhaohui Sunny Zhou, PH.D. in support of IPR2025-01346
1085	<i>Curriculum Vitae</i> of Dr. Zhaohui Sunny Zhou, Ph.D.
1086	Ryan Davis, <i>PTAB Leader Urges Specificity in Discretionary Denial Briefs</i> , https://www.law360.com/ip/articles/2385678?nl_pk=b8251133-4cde-4950-bff3-e7ef91a38c23&utm_source=newsletter&utm_medium=email&utm_campaign=ip&utm_content=2025-09-10&read_main=1&nlsidx=0&nlaidx=0?copied=1
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Exhibit No	Description
1089	Eli Lilly And Company FORM 10-Q for the quarterly period ending September 30, 2025.
1090	Eli Lilly And Company FORM 10-K for the fiscal year ended December 31, 2024.
1091	DeFosse et al., Data Undermines USPTO’s ‘Settled Expectations’ Doctrine
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I. INTRODUCTION

BPI Labs, LLC (“Petitioner”) submits that the present proceeding exemplifies why the Acting Director’s March 26, 2025, *Process Memorandum on Bifurcated Discretionary Denial Review* (“the Stewart Memo”), was issued, namely, to ensure that meritorious petitions are not denied on procedural grounds divorced from fairness, public policy, and the realities of the patent system. Ultimately, the facts and law converge on one outcome, that the Director should institute IPR despite any countervailing factors. *Dabico Airport Sols. Inc. v. AXA Power ApS*, IPR2025-00408, Paper 21 at 2-3 (Director June 18, 2025) (“parties are encouraged to address any fact or circumstance they believe bears on whether the Office *should* or should not institute trial”) (emphasis in original) (internal quotes omitted).

Notably, the Deputy Director previously considered arguments by Eli Lilly & Co. (“Patent Owner”) and Empower Clinical Services related to U.S. 9,474,780 (“the ’780 Patent”). *Empower Clinical Services, LLC v. Eli Lilly & Co.*, IPR2025-01024, Paper 15. In her decision, the Deputy Director determined that, while some factors weigh against discretionary denial, those factors were outweighed by the Patent Owner’s settled expectations favoring discretionary denial. *Id.* at 2-3. Importantly, however, the Deputy Director determined that, other than contesting Patent Owner’s settled expectations, Empower did “not otherwise provide persuasive reasoning why an *inter partes* review is an appropriate use of Board resources.” *Id.* Unlike in that

case, Petitioner here presents new arguments and evidence establishing why IPR is an appropriate use of Board resources.

First, the regulations related to compounding create well-established expectations for Petitioner and other compounding pharmacies. When the FDA added tirzepatide to its Section 506E drug shortage list in December 2022, Petitioner responded decisively by making substantial investments to produce compounded tirzepatide to meet urgent patient demand due to Patent Owner's failure to adequately invest in manufacturing. Petitioner's swift actions and substantial investments in these compounded medications ensured the continued health of patients.

The FDA removed tirzepatide from the shortage list in late 2024. Despite its removal, compounding of "non-essential copies" of tirzepatide continues in order to meet specific patient needs. Patent Owner has aggressively filed a string of lawsuits aimed at ending that compounding and reestablishing its monopoly over tirzepatide, but has not asserted the '780 Patent in any of those suits, shielding it from challenge. Petitioner, the compounding industry generally, and the patients they serve deserve clarity regarding the legal rights of compounders to continue producing tirzepatide after the substantial investments they made.

Second, settled expectations for patent owners who have patents covering FDA-approved pharmaceutical products differ markedly from those of typical patent

holders.² Indeed, as one of Patent Owner’s big pharma competitors recently observed, “pharmaceutical patents are often challenged much later in their lifespan compared to other industries, since generic companies develop competing products only after a branded drug has been on the market for some time.” Ex. 1086 (quote by Amgen’s senior counsel).

The Hatch-Waxman Act (formally, the Drug Price Competition and Patent Term Restoration Act of 1984; 35 U.S.C. § 271(e)(2)(A)) provides the statutory mechanisms and requirements under which generic drug manufacturers may file a generic drug application with the FDA (known as an abbreviated new drug application or “ANDA”) to seek approval for generic versions of branded drug products. ANDA applications may include a “Paragraph IV” certification where the generic applicant asserts that one or more patents listed in FDA’s Orange Book as covering the branded product are invalid or not infringed. Under the provisions of the Hatch-Waxman Act, the mere act of filing an ANDA containing a Paragraph IV

² Petitioner maintains that the clock for determining when Settled Expectations attach for the ’780 Patent should not begin until May 13, 2022, at the earliest (i.e., only after a certain amount of time after May 13, 2022 can Settled Expectations be established). Petitioner also observes that, in a study of IPRs filed since 2012, 46.6% of IPRs (8,166 out of 17,515 petitions) were filed against patents in force for six or more years, and, of these petitions that reached a final written decision, 82% resulted in cancellation of at least one claim. Ex.1091 at 2-3. Thus, Patent Owners should expect that patents that have been in force for more than 6 years may face invalidity challenges.

certification is deemed an artificial act of patent infringement in order to create the necessary case or controversy that allows a lawsuit to be filed in District Court, and for the validity of the Orange Book patent(s) to be adjudicated.

The '780 Patent, which is directed to the tirzepatide compound itself, is an Orange Book listed patent for two of Patent Owner's products: Mounjaro[®] (for type 2 diabetes) and Zepbound[®] (for obesity and obstructive sleep apnea). However, because tirzepatide is a "new chemical entity" (i.e., an active chemical moiety that has not been previously approved in any New Drug Application (NDA) under 21 U.S.C. §355), Mounjaro[®] and Zepbound[®] are entitled to data exclusivity for a period of five years after the approval date of the first approved product, which in this case was May 13, 2022. *See* EX1087 and EX1088. Based on this data exclusivity, a generic manufacturer cannot even file an ANDA for a generic version of either Mounjaro[®] or Zepbound[®] until **May 13, 2026**, at the earliest (i.e., four years after the approval date). *See* 21 U.S.C. § 355(c)(3)(E). Without the filing of the ANDA, there is no case or controversy upon which District Court litigation can be initiated. Consequently, a drug manufacturer has only two options for initiating a proceeding that would allow it to challenge the validity of an Orange Book patent such as the '780 patent based on the prior art: (1) file an ANDA (which is not an option until at least May 13, 2026); or (2) file a challenge at the USPTO. The Hatch-Waxman statutory framework shields the '780 Patent from being challenged in District Court,

and the Patent Owner now seeks to improperly extend that embargo to the USPTO by seeking a discretionary denial.

Indeed, Deputy Director Stewart has expressly acknowledged that certain situations and industries weigh against settled expectations, and justify review of challenged claims years after issuance. Deputy Director Stewart has stated that “a patent may have been in force for years but may not have been **commercialized, asserted, marketed, licensed, or otherwise applied** in petitioner’s particular technology space, if at all[,] [t]hese non-exclusive examples provide considerations that weigh against a patent owner’s claim of settled expectations and bears on the Director’s discretion.” *Intel Corp. v. Proxsense LLC*, IPR2025-00327, -00328, and -00329, Paper 12 at 2-3 (emphasis added). Prior to the first FDA approval on May 13, 2022, there was no commercialization, assertion, or marketing of the ’780 patent. Thus, the clock for settled expectations for the ’780 patent should not begin ticking until at least the date of first FDA approval.

Third, Patent Owner tries to circumvent the process laid out by the Stewart Memo by arguing that Petitioner should have argued discretionary issues related to 35 U.S.C. § 325(d) in its Petition and inserts merits-based positions in its discretionary denial brief. Of course, under the bifurcated process laid out by the PTAB, Petitioner should not address discretionary denial factors until its authorized opposition paper, namely this brief.

II. IPR IS AN APPROPRIATE USE OF BOARD RESOURCES TO PROVIDE CLARITY AND TO PROMOTE LOWER DRUG COSTS

Patent Owner wields the '780 Patent as a sword that hangs over the head of every compounder of tirzepatide, and that threatens to reduce competition and burden patients and payors with Lilly's monopoly pricing. Lilly currently rakes in approximately \$7 billion in U.S. sales for its tirzepatide products per quarter. Ex. 1089 at 13; *See also* Ex. 1090 at 41 ("increasing revenue in 2024 was driven primarily by Mounjaro, Zepbound, and Verzenio..."). Although Patent Owner complains about the compounders who have been able to provide extraordinary cost savings and meet unique patient needs, Patent Owner has thus far refused to assert the '780 Patent against any compounder of tirzepatide, as doing so would open the '780 Patent's validity to adjudication via a District Court.

Instead of subjecting the '780 Patent to adjudication, which would bring clarity to the compounding industry and the patients that rely on compounded products, Patent Owner instead has employed a strategy that attempts to insulate the '780 Patent from any review. Specifically, Patent Owner has filed more than 30 lawsuits against tirzepatide compounders throughout the country, asserting Lanham Act and state false advertising claims in an attempt to stifle competition, but as of yet has not asserted infringement of the '780 Patent despite the clear option to do so.

Petitioner and others made substantial investments in the manufacture and distribution of tirzepatide. Petitioner's past, current, and future investments are now

at risk in view of Patent Owner's aggressive enforcement against compounders of tirzepatide, while purposefully withholding adjudication of the '780 Patent, which creates a cloud of uncertainty for Petitioner, other compounders, and the patients who rely on compounded products to meet their unique needs.

While the '780 Patent can be challenged in *ex parte* reexamination, the subject matter here is complex (nearly 100 exhibits were filed with the Petition), and the Office would benefit from the ongoing adversarial participation of both parties with depositions of each party's experts – features not available in *ex parte* reexamination. In addition, *ex parte* reexamination does not have statutory deadlines and thus cannot provide the clarity in timing of reaching a final decision.

Therefore, Patent Owner's aggressive enforcement against the tirzepatide compounding industry, combined with its refusal to adjudicate the '780 Patent in those same actions, gives rise to the need for the Office to consider the validity of the '780 Patent at this time to provide clarity to compounders and the patients they serve. Indeed, IPR is the only currently available adversarial proceeding to obtain this clarity. See IPR2025-01024, Paper 15 at 2-3 (Petitioner can provide "persuasive reasoning why an *inter partes* review is an appropriate use of Board resources" to overcome discretionary denial).

III. PETITIONER'S SETTLED EXPECTATIONS COUNTER-BALANCE OR OUTWEIGH PATENT OWNER'S SETTLED EXPECTATIONS

In IPR2025-01024, the Deputy Director determined that Patent Owner's

settled expectation outweighed other factors in deciding to discretionarily deny that IPR petition. IPR2025-01024, Paper 15 at 2-3. In particular, the Deputy Director noted the Patent Owner's investment in clinical studies related to tirzepatide. However, Petitioner raises two further issues not considered in IPR2025-01024 that should result in a different outcome here: (1) Petitioner made significant investments in the manufacture and distribution of tirzepatide to help address the FDA-mandated shortage that was caused by Patent Owner's failure to adequately invest in the same; and (2) under the Hatch-Waxman Act regime and the unique realities of the pharmaceutical industry, the clock for determining whether a Patent Owner has established settled expectations on a patent covering an FDA-approved pharmaceutical product should not begin until at least the first date of FDA approval.

A. Petitioner's Investment During the FDA Shortage Created Settled Expectations for the Petitioner

FDA added tirzepatide to its drug shortage list in December 2022 and removed it in late 2024. To address the Patent Owner's failure to sufficiently invest in manufacturing to meet demand, Petitioner and other compounders made investments in manufacturing and distribution of tirzepatide to ensure patients' steady access. And, Petitioner continues to use its investments to make a "non-essential copy" of Lilly's tirzepatide products to meet special patient needs.

Patent Owner now threatens these significant investments. Since FDA declared an end to the shortage, Patent Owner has made clear its intent to undermine

compounders' investments through vexatious lawfare by filing suits on only certain claims (i.e., Lanham Act) while keeping other claims (i.e., patent) in reserve, should its first round of attacks fail. Patent Owner's market cap is near one trillion dollars, and there is little doubt it can spend inordinate sums of money over the next decade, bringing lawsuit after lawsuit against Petitioner and others in the compounding industry. This IPR will provide a resolution to the industry of Patent Owner's '780 Patent, removing the cloud over patient access to these legally marketed products. In sum, Petitioner has settled expectations to enjoy the fruits of its investments in tirzepatide without the un-ending risk of lawsuits from Patent Owner's deep pockets.

B. Settled Expectations for Patents on FDA-Approved Medications Differ From Those in Other Industries

The '780 Patent was issued in 2016, but tirzepatide first received FDA approval on May 13, 2022, and was granted five years of New Chemical Entity ("NCE") exclusivity. As a result, no generic competitor can challenge the '780 patent via the statutory mechanisms provided by the Hatch-Waxman Act until May 13, 2026, the earliest date FDA can accept an ANDA filing. Using a patent's issue date to assess settled expectations disregards the practical realities of generic and compounding drug development, unfairly prejudicing petitioners in this industry and undermines the purpose of IPR proceedings.

Reliance on a patent's issue date to assess settled expectations assumes that patent owners and competitors can act immediately upon issuance. In non-

pharmaceutical contexts, this may hold true, as competitors can develop products or challenge patents without regulatory gatekeepers. However, in the pharmaceutical industry, the Hatch-Waxman framework disrupts this basic assumption. In fact, the Hatch-Waxman framework blocks generic applicants from even filing an ANDA for four years after approval of a brand product (also known as the Reference Listed Drug or “RLD”) containing an active ingredient not previously approved by the FDA. *See* 21 U.S.C. § 355(c)(3)(E). Thus, generic companies are statutorily blocked from challenging patents covering a brand product for years, often more than a decade, after the patents issued. Indeed, the ’780 patent issued October 25, 2016, more than five years prior to FDA approval of tirzepatide on May 13, 2022.

Although compounders are not governed by the strict timelines of the Hatch-Waxman Act, brand pharma companies also do not have any expectation of their patents being challenged by compounders prior to FDA approval. This is because prior to FDA approval there is no need to compound alternative doses, dosage forms, or formulations of a branded drug product to meet specific patient needs. Nor can a shortage of the branded drug product exist prior to FDA approval.

Using the patent issue date as the benchmark for settled expectations thus creates an inequitable standard in this industry. It assumes generics and compounders could have challenged the patent earlier, ignoring the regulatory reality that ANDA preparation and/or the development of a compounded product—and thus the

incentive to challenge key patents—only crystallizes post-FDA approval. This misapplication of settled expectations in this industry risks denying meritorious IPR petitions, shielding potentially invalid patents from scrutiny, and contravening the America Invents Act’s purpose of promoting patent quality. *See Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2139 (2016) (citing 157 Cong. Rec. 9778 (2011) (remarks of Rep. Goodlatte) (noting that *inter partes* review “screen[s] out bad patents while bolstering valid ones”).

FDA approval is the pivotal moment when generic companies and compounders can advance development of their products, making it the appropriate benchmark for settled expectations. Prior to approval, companies lack access to the RLD’s final formulation, dosing, and labeling, which are critical for product development, bioequivalence studies, and ANDA preparation. *See* 21 C.F.R. § 320.21 (bioequivalence requirements).

In view of these stark realities, generics and compounders have no need to consider legal challenges to key patents covering the branded product until after FDA approval. This is underscored by the fact that 90% of clinical drug candidates that reach Phase I clinical trials fail during the development process (e.g., fail due to a lack of safety and/or efficacy during Phase I, II, or III clinical trials, all of which are required as part of the FDA approval process). *See* Ex. 1092. Given this high failure rate and uncertainty, no generic competitor or compounder can reasonably

commit the necessary resources to develop a product (including assessment of legal challenges), until the branded product survives clinical development and obtains FDA approval.

Indeed, in IPR2025-00408, Deputy Director Stewart noted that “there is no bright-line rule on when expectations become settled,” but that the approach should “align[] with other approaches to settled expectations and incentives, for example, for filing infringement lawsuits.” Cf. 35 U.S.C. §286 (‘Except as otherwise provided by law, no recovery shall be had for any infringement committed more than six years prior to the filing of the complaint or counterclaim for infringement in the action.’).” *Dabico Airport Sols. Inc. v. AXA Power ApS*, IPR2025-00408, Paper 21 at 3. Deputy Director Stewart indicated that the 6-year window for when settled expectations attach to a patent should align with the 6-year window for when a patent owner can claim damages for previous infringement.

Prior to FDA approval of the tirzepatide products on May 13, 2022, there could be no competing tirzepatide products, meaning that the earliest the 6-year window for assessing damages based on infringement of the then FDA-approved tirzepatide products could begin was May 13, 2022, the same date that the clock for settled expectations should begin in this case. Tying settled expectations to the FDA approval date rather than a patent’s issue date, reflects this timeline and these realities, ensuring generics and compounders have a fair opportunity to challenge

patents once regulatory hurdles are lifted.

Patent Owner was thus aware that its patents would be protected from validity challenges for much of their effective life, far longer than patent holders outside of the pharmaceutical industry typically enjoy. This strategic insulation from validity challenges undermines the argument for relying on settled expectations of six years from a patent's issue date for patents covering FDA-approved pharmaceutical products.

As such, when viewed in the light of a holistic, context-sensitive analysis, it becomes clear that Patent Owner does not enjoy settled expectations in the '780 Patent in the same way as patent owners in other industries. Accordingly, Patent Owner's claim to settled expectations against validity challenges to the '780 Patent are *de minimis*, if any exist at all.

IV. PATENT OWNER'S PREVIOUSLY FAILED ARGUMENTS REGARDING *ADVANCED BIONICS* ARE NOT PERSUASIVE

Patent Owner spends much of its discretionary denial brief arguing that the instant IPR petition should be denied under the *Advanced Bionics* framework as raising "substantially the same prior art or arguments" previously presented to the Office. *See Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (P.T.A.B. Feb. 13, 2020) (precedential); 35 U.S.C. § 325(d). Patent Owner raised almost the exact same arguments in IPR2025-01024, yet the Deputy Director did not cite this argument in her decision. These arguments

are no more persuasive here than they were in IPR2025-01024.

A. Prior Art Was Not Previously Considered Under *Advanced Bionics* Step one

Here, there is little dispute that the relevant teachings of Lau presented in the Petition were not considered during prosecution. For Alsina-Fernandez, Patent Owner relies on a misguided theory that mere mention of a reference in the specification should render all the subject matter of that reference deemed considered even though that contradicts MPEP policy guidelines. Because at least these references and their relevant teachings have never been considered before, the Director need not even consider step two of *Advanced Bionics*.

1. *Lau was never considered*

Lilly does not contend that Lau was ever considered by the Office previously but instead argues that it is cumulative because the compound of “semaglutide” was considered and/or is cumulative to the conjugation of Just. PO DD Req. at 13. But, Lau teaches much more.

Petitioner relies on Lau to teach “Gly at position 29,” “peptide design choices to prolong half-life and extend dosing frequency,” “conjugating the lysine residue in position 20...of GLP-1 to an albumin-binding moiety that increases the duration of action of the GLP-1 analogue,” “prolonging the action of the agonist is applicable...to other peptides,” “the acylated GLP-1 analogues can bind to albumin and the GLP-1 receptor simultaneously,” “preferred substitutions at the 7 and/or 8

position, preferably Aib (α -aminoisobutyric acid) at position 8,” “the spacer is a ‘hydrophilic linker’ that separates the peptide and the albumin binding residue,” and “the inclusion of the same [2-(2-Amino-ethoxy)-ethoxy]-acetyl)-2-(γ Glu) spacer (also known as an AEEA-AEEA- γ Glu spacer) to attach the fatty acid (of various lengths) to the lysine at the 20 position of the peptide.” See Petition at 45; 51-53; 57-59.

Patent Owner does not attempt to map where these teachings are found in the structure of semaglutide or the conjugation of Just. Lau’s teachings help inform a POSA of the modifications that are proposed in the Petition, and there is no dispute that these teachings were not before the examiner during prosecution. See *Oticon Medical v. Cochlear Ltd.*, IPR2019-00975, Paper 15 at 16 (PTAB 2019) (precedential as to § II.B and II.C, Mar. 24, 2020) at 16 (new prior art teachings related to motivation considered in *Advanced Bionics* step one).

2. *Alsina-Fernandez was never considered*

Lilly argues Alsina-Fernandez should be deemed considered because it is cited in the specification, even though it was not identified in an IDS. PO DD Req. at 10-11. Yet, the MPEP provides that “MPEP § 609 sets forth guidelines for applicants, their attorneys and agents who desire to submit prior art for consideration by the U.S. Patent and Trademark Office.” MPEP §§707.05(b). MPEP §609, in turn explains how an Information Disclosure Statement (IDS) is the vehicle for an

Applicant to identify references for an Examiner's consideration. MPEP §609; 37 C.F.R. §1.97.

Patent Owner failed to list Alsina-Fernandez in an IDS despite the obligations imposed by regulation and the MPEP. *See* 37 C.F.R. §1.98(a)(1); MPEP §609. The USPTO similarly requires the examiner to identify references considered during examination in addition to those listed on the Applicant's IDS(s). MPEP §707. Here, there is no evidence that the examiner ever identified Alsina-Fernandez on form PTO-892 or otherwise as being a reference considered.

Lacking evidence of actual consideration by the examiner, Patent Owner points to non-precedential decisions to wrongly assert that a reference listed in the specification but not provided on an IDS is "considered" with respect to *Advanced Bionics* step one. Patent Owner DD Req. at 11. Yet, Patent Owner's rationale is expressly contradicted by the MPEP, which states that listing references for consideration by the examiner "may not be incorporated into the specification of the application in which it is being supplied, but must be submitted in a separate paper" that enables the "examiner to indicate which identified documents have been considered." MPEP §609.04(a)(I) (emphasis added). Patent Owner cannot now assert that its failure to follow Patent Office procedure to have a reference considered should be deemed as a fact in its favor.

Patent Owner lastly argues that Alsina-Fernandez is cumulative to the Just

reference considered by the Examiner during prosecution simply because both would require “modifications” to arrive at the claimed invention. PO DD Req. at 11-12. This argument fails on its face because it would mean that any prior art used for a combination under Section 103 is cumulative (because any prior art used for an obviousness combination would require “modifications” to arrive at the claimed invention). Notably, Patent Owner does not even allege that the two references require the same modifications (as they would not).

B. Examiner Materially Erred Under *Advanced Bionics* Step Two

If *Advanced Bionics* step two even needs to be considered, the Deputy Director recently determined that “the second part of *Advanced Bionics* [is satisfied] because the asserted prior art was not a basis for rejection during examination, is not substantially the same as prior art the Examiner applied, and includes specific teachings that ‘impact patentability of the challenged claims.’” *Ecto World, LLC v. Rai Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 5 (USPTO Dir. 2025) (precedential) (quoting *Advanced Bionics* at 8 n.9). “A petitioner also may point to the fact that even though the asserted prior-art is listed on an IDS, the Examiner did not issue any prior-art rejections during examination, so the Examiner materially erred by overlooking certain teachings in the prior art on the IDS.” *Id.* at 5-6.

This is precisely the case here, as there were no rejections during prosecution based on Alsina-Fernandez, DiMarchi, Lau, or any other prior art. As discussed with

respect to step one, Patent Owner has also not shown that any of the teachings that the Petition relies on from Lau or Alsina-Fernandez are cumulative with the prior art that the examiner did consider. Finally, as explained in the Petition, the teachings of the prior art cited in the Petition impact the patentability of the challenged claims.

Indeed, the Deputy Director has repeatedly concluded that it was material examination error to allow claims where the teachings of other references not considered by the examiner taught relevant features of the claims. *See Microsoft Corp. v. X1 Discovery, Inc.*, IPR2025-00253 Paper 13 at 2 (USPTO Dir. 2025); *Xencor, Inc. v. Merus N.V.*, IPR2025-00604 Paper 12 at 2-3 (USPTO Dir. 2025). Therefore, the failure of the examiner to consider the references, and particularly the combination that is presented in the Petition, is material error.

V. PATENT OWNER’S “WEAK” LABEL FAILS IN LIGHT OF THE PARALLEL PETITION’S STRONG SUBSTANTIVE SHOWINGS

In a last-ditch effort to avoid review of its patent, Patent Owner argues that the Petition should be discretionarily denied because of its “weak merits.” PO DD Req. at 15-19. But, in making this argument, Patent Owner paints with a broad brush and glosses over the detailed arguments and evidence presented in the Petition and Zhou Declaration. For example, Patent Owner argues that “Petitioner does not even *attempt* to show why a skilled artisan would have chosen Example 2 of Alsina-Fernandez over any of the numerous GIP/GLP-1 dual agonists” *Id.* at 16 (emphasis in original). Yet, the Petition explains over the course of multiple pages

(with significant citations to the prior art and Zhou Declaration) why a POSA would have (i) looked to Alsina-Fernandez given its teachings on the benefits of co-GLP-1/GIP agonists and (ii) focused in particular on Example 2 as a lead compound given its reported promising dual agonism properties and selectivity. Petition at 30-42.

The Patent Owner's hyperbolic argument that Petitioner's "expert fails to provide **any** reason a skilled artisan would choose Alsina-Fernandez for the lead compound selection over **any** other reference disclosing GIP/GLP-1 dual agonists" (PO DD Req. at 16-17; emphasis in original) fares no better. In fact, Dr. Zhou explains this exact issue in great detail over the course of twelve pages in his declaration. Ex. 1084 at ¶¶117-138. And, contrary to Patent Owner's restrictive view of the law, the Federal Circuit has made it clear that the lead compound can be one of a group of promising compounds and that the prior art need not "point to only a single lead compound for further development efforts, that restrictive view of the lead compound test would present a rigid test similar to the teaching-suggestion-motivation test that the Supreme Court explicitly rejected in KSR." *Altana Pharma AG v. Teva Pharmaceuticals USA, Inc.*, 566 F.3d 999, 1008–09 (Fed. Cir. 2009).

Patent Owner's exaggerations only get worse when it argues that the Petition should be discretionarily denied because only a few cases have invalidated compound patents. PO DD Req. at 18-19. Even if that were true, that only goes to the strength and novelty of other compound patents. As demonstrated in the Petition

here, a POSA was motivated to follow the path made clear by the prior art to modify the lead compound set out in Example 2 of Alsina-Fernandez in such a way as to arrive at the compound in the challenged claims with a reasonable expectation of success. What has happened in other cases involving different compounds and different prior art has little bearing on the merits here.

VI. CONCLUSION

For the foregoing reasons, Petitioner respectfully requests that the Director not discretionarily deny the petition.

Dated November 12, 2025,

Respectfully submitted,

/James P. Murphy/

James P. Murphy

Reg. No. 55,474

Polsinelli PC

1000 Louisiana Street

Suite 6400

Houston, Texas 77002

Tel: (713) 374-1600

Corey Casey

Reg. No. 66,950

Polsinelli PC

900 West 48th Place

Suite 900

Kansas City, Missouri 64112

Tel: (816) 572-4439

Chad Landmon
Pro Hac Vice (pending)
Polsinelli PC
1401 I St NW
Suite 800
Washington, DC 20005
Tel: (202) 626-8303

Attorneys for Petitioner

CERTIFICATE OF SERVICE UNDER 37 CFR § 42.6(e)(4)

The undersigned hereby certifies that a copy of the foregoing Petitioner's Opposition to Patent Owner's Brief on Discretionary Denial, is being served on November 12, 2025, via email directed to the following counsel of record for the Patent Owner:

Michael A. Morin
michael.morin@lw.com

David P. Frazier
david.frazier@lw.com

Michelle L. Ernst
michelle.ernst@lw.com

Inge A. Osman
inge.osman@lw.com

Danica Hostettler
dhost@lilly.com

Aaron F. Barkoff
barkoff_aaron@lilly.com

/Ericka McNeil/
Ericka McNeil
Polsinelli, PC
1000 Louisiana Street, Suite 6400
Houston, Texas 77002
Tele: (713) 374-1600