

Case No. PGR2025-00057

Patent No. 12,234,236

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CONJUPRO BIOTHERAPEUTICS, INC.,
Petitioner,

v.

ASCLETIS PHARMA CHINA CO. LTD.,
Patent Owner.

Case No. PGR2025-00057

Patent No. 12,234,236

Title: GLP-1R agonist and therapeutic method thereof

**PATENT OWNER'S BRIEF IN SUPPORT OF
DISCRETIONARY DENIAL**

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Exhibit	Description
EX2002	Excerpts of File History of U.S. Patent No. 12,234,236
EX2003	Excerpts of File History of U.S. Patent Application No. 18/885,065
EX2004	International Publication No. WO 2025/131043A1
EX2005	Certified English Translation of International Publication No. WO 2025/131043A1
EX2006	U.S. Patent No. 12,291,530

I. INTRODUCTION

Conjupro's Petition is simply a case of sour grapes. Conjupro filed this Petition only after Ascleitis rejected Conjupro's unsolicited request to license the challenged patent, which it sought because real-party in interest CSPC is developing oral GLP-1 agonists. (Pet. 5.) Indeed, while Petitioner now asserts the claimed compounds are obvious, CSPC filed a patent application on oral GLP-1 agonists with a *later priority date* that claims one of the *exact same compounds*, the '236 patent's Compound 1, presumably to cover its own clinical candidate. (EX2004; EX2005 (certified translation), 1, 95-96.) Petitioner failed to tell the Office about its patent application in the Petition, likely because it shows CSPC believed the claimed compounds were novel and non-obvious prior to learning that Ascleitis first invented and filed on them.

Now, unable to clear its way to market with a license, Petitioner asks the Office to find the challenged claims unpatentable based on art and arguments recycled from prosecution. Indeed, the Examiner expressly allowed the claims over one of Petitioner's primary references, Yoshino. Petitioner's other primary reference, Su, is cumulative of Yoshino, as Petitioner's own arguments show. The secondary references likewise were considered by the Examiner or are cumulative. As to Examiner error, Petitioner's conclusory one page discussion does not come close to meeting its burden on that issue, particularly given that the Examiner

expressly allowed the claims over Yoshino and later explicitly allowed related U.S. Patent No. 12,291,530 over Su.

Under Section 325(d), the Board should deny institution because the same or substantially the same prior art or arguments raised in the Petition were previously presented to and rejected by the Office without any showing of Examiner error.

II. ARGUMENT

A. The Office Should Exercise Its Discretion to Deny the Petition Under § 325(d)

“In determining whether to institute or order [a post-grant review], 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.” 35 U.S.C. § 325(d). In evaluating § 325(d), the Office considers the framework articulated in *Advanced Bionics*, which sets forth a two-part inquiry: (1) whether the same or substantially the same art or arguments were previously presented and (2) if so, whether the petitioner has demonstrated that the Office materially erred in its prior consideration of that art or those arguments. *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 7-11 (PTAB Feb. 13, 2020) (precedential); *Ecto World, LLC, et. al. v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 2-7 (PTAB May 19, 2025). “At bottom, this framework reflects a commitment to defer to previous Office

evaluations of the evidence of record unless material error is shown.” *Advanced Bionics*, Paper 6 at 9.

One of Petitioner’s primary references, Yoshino, was raised by the Examiner in the Notice of Allowance. The other primary reference, Su, is cumulative of Yoshino and other prior art, and the Petition provides no analysis to the contrary. The secondary references were cited on Information Disclosure Statements (“IDSs”) and/or identified in the Examiner’s search report (Kawai, Bethel, Meng, Ren) or are cumulative of other cited prior art (Talele, Patel, Pennington). Moreover, the Examiner did not err in considering the cited prior art, and Petitioner’s own patent application shows it believed the claimed compounds were novel and non-obvious. The Office should exercise its discretion to deny this Petition under § 325(d).

1. Grounds 1 and 2 Fail the *Advanced Bionics* Framework

Ground 1 relies on “Su, Yoshino, and Kawai, in view of Talele,” and Ground 2 relies on “Yoshino and Kawai in view of Talele.” (Pet. 7.) The Office should exercise its discretion to deny institution based on Grounds 1 and 2 because they present the same or substantially the same art and arguments previously presented to the Office, and Petitioner has not demonstrated any material error as to the patentability of the challenged claims.

a. Grounds 1 and 2 Rely on the Same or Substantially the Same Art Considered During Prosecution

The first part of the *Advanced Bionics* framework examines “whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office.” *Advanced Bionics*, Paper 6 at 8. “Previously presented art includes art made of record by the Examiner, and art provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent.” *Id.* The Petition’s four references for Grounds 1 and 2 (Yoshino, Kawai, Talele, and Su) were all before the Examiner or are substantially the same as art before the Examiner.

Yoshino and Kawai were considered during prosecution. The Petition, as it must, acknowledges that Yoshino was considered during prosecution. (Pet. 117-18.) In fact, Yoshino was one of only thirty-nine references that resulted from the Examiner’s search based on the core structure of orforglipron, a prior art GLP-1 agonist. (EX2002, 312-839.) The search report included 156 pages identifying various structures and disclosures from Yoshino, including most of the structures from Yoshino relied on in the Petition. (EX2002, 681-836, 686 (Yoshino Compound 67), 788 (Yoshino Compound 40), 697 (Yoshino Compound 22), 721 (Yoshino Compound 64), 705 (Yoshino Compound 35), 701 (Yoshino compound 28), 707 (Yoshino Compound 38), 702 (Yoshino Compound 30).) In addition, the patentees

disclosed the PCT publication that led to Yoshino in an IDS, and the Examiner indicated he considered that reference. (EX2002, 865 (citing WO 2018/056,453).)

After his review, the Examiner allowed the claims and found that “Claims 1-25 are patentable over Yoshino” in the Notice of Allowance. (EX2002 at 845.) That is more than sufficient to satisfy the first part of the *Advanced Bionics* framework for Yoshino. *Advance Medical Designs Inc. v. Corbin Clinical Resources, LLC*, PGR2023-00041, Paper 12 at 23-25 (PTAB Jan. 23, 2024) (concluding the first part of the *Advanced Bionics* framework was satisfied for a prior art reference cited by the examiner in the Notice of Allowance).

Kawai was also considered during prosecution. The patentees cited Kawai in an IDS, and the Examiner indicated he considered the reference. (EX2002, 278, 871.) Kawai was also one of the thirty-nine references in the Examiner’s search report. (EX2002, 679.) The first part of the *Advanced Bionics* framework is thus satisfied for Kawai. *Ecto World*, Paper 13 at 4 (“Challenging the claims using the same prior art that was previously presented on an IDS is sufficient to satisfy the first part of the *Advanced Bionics* framework.”); *Keysight Techs., Inc. v. Centripetal Networks, Inc.*, IPR2022-01421, Paper 14 at 5 (PTAB Aug. 24, 2023) (“The first part of the *Advanced Bionics* framework does not require that an Examiner provide a discussion, analysis, or other findings on the applicability of the relevant material contained in an IDS.”).

Petitioner incorrectly argues that Yoshino and Kawai were not considered because of the timing of the IDSs relative to the Notice of Allowance, the number of prior art references cited, and the alleged lack of evidence that the Examiner considered Yoshino's Compound 67. (Pet. 117-18.) The Petitioner cites no authority to support its argument and, to the contrary, the Office's precedent is clear that citation in an IDS, Notice of Allowance, or search report is, by itself, sufficient to satisfy *Advanced Bionics* Part 1. See, e.g., *Ecto World*, Paper 13 at 4; *Keysight Techs.*, Paper 14 at 5; *Advance Medical Designs*, Paper 12 at 23-25.

Moreover, Petitioner's suggestion that the Examiner did not consider these references is factually wrong. The Examiner initialed IDSs disclosing the PCT publication that led to Yoshino and Kawai, indicating that the Examiner considered those references. (EX2002, 865, 871.) And both references had already appeared in the Examiner's search report. (EX2002, 679, 757.) Petitioner's conjecture that the Examiner did not consider those references, despite the evidence otherwise, is just that: pure conjecture. See *Sketchers U.S.A., Inc. v. Nike, Inc.*, IPR2025-00141, Paper 20 at 13 (PTAB June 3, 2025) (citing the examiner's "notation at the bottom of the page: 'ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH./M.P./'" in concluding that the first part of the *Advanced Bionics* framework is satisfied for a prior art reference).

Talele and Su are cumulative. Talele and Su are each cumulative of art that was before the Examiner during prosecution. *See Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17 (PTAB Dec. 15, 2017) (precedential) (relevant considerations include “the similarities and material differences between the asserted art and the prior art involved during examination” and “the cumulative nature of the asserted art and the prior art evaluated during examination”).

As an initial matter, Petitioner fails to meet its burden to show that Talele and Su are not cumulative. *Parse Biosciences, Inc., v. 10X Genomics, Inc.*, IPR2023-01033, Paper 8 at 14 (PTAB Dec. 19, 2023). The Petition generically states that Talele and Su disclose “compounds materially distinct from the sole compound cited in the Notice of Allowance” and “motivations to combine or modify the references and other knowledge of a POSA that renders the claims of the ’236 Patent obvious.” (Pet. 118.) But the Petition does not (1) make any comparison of Talele and Su to **all of** the prior art considered during prosecution (*i.e.*, not just “the sole compound cited in the Notice of Allowance”); (2) explain how the compounds disclosed in those references are allegedly “materially distinct” from the considered prior art; or (3) articulate the “different motivations to combine or modify” they allegedly teach. (Pet. 118.) The Petition’s failure to provide any substantive cumulateness analysis by itself is fatal on *Advanced Bionics* Part 1. *Parse Biosciences*, Paper 8 at 14

(“Petitioner’s failure to conduct *any* analysis of whether its art was cumulative is, by itself, fatal under AB part one.”); *see also Alarm.com, Inc. v. Vivint, Inc.*, IPR2022-00728, Paper 6 at 20 (PTAB Nov. 1, 2022) (discretionarily denying institution where “Petitioner does not address the similarities between [references], applied during prosecution of the challenged claims, and [the reference] relied upon in each of the asserted grounds.”).

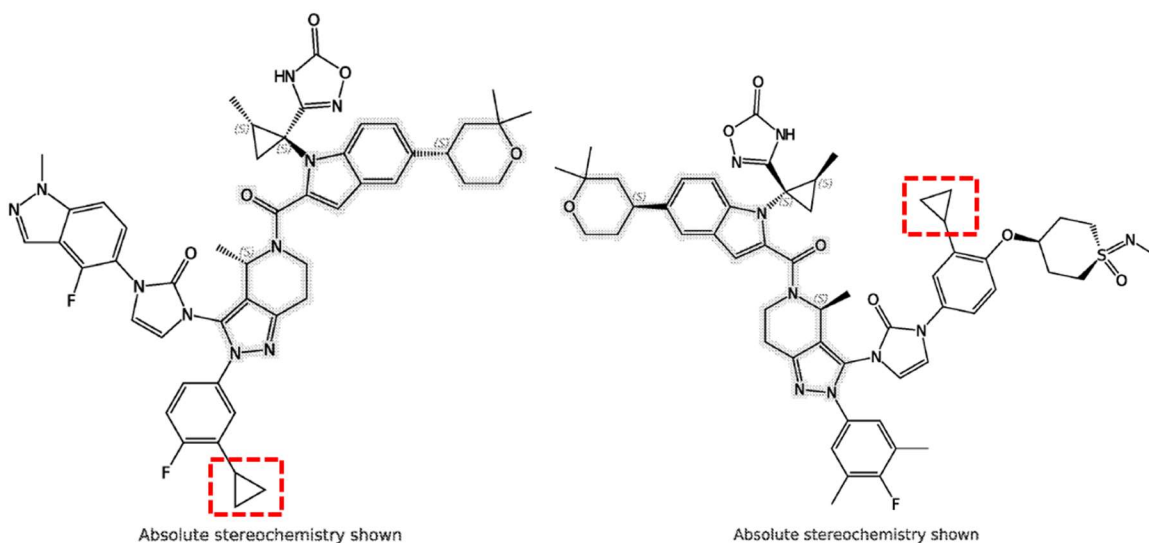
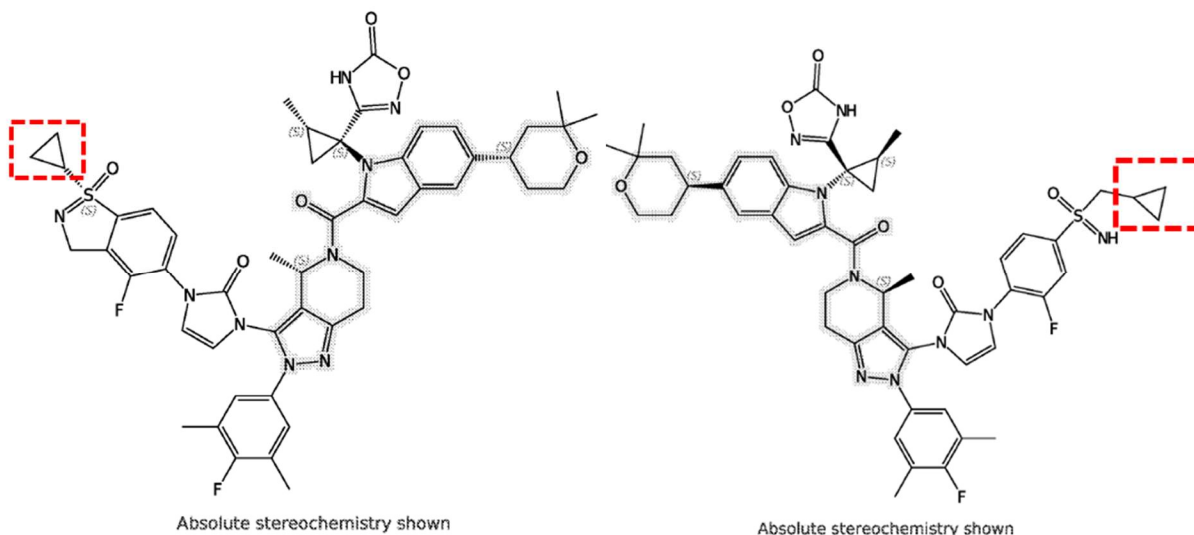
Even if Petitioner’s failure to meet its burden was not determinative (and it is), *Advanced Bionics* Part 1 is satisfied because Talele and Su are cumulative.

Talele. Talele was not cited during prosecution or identified by the Examiner because it has nothing to do with orforglipron or GLP-1 agonists. Instead, Talele is a review article that generally discusses the use of cyclopropyl ring structures in unrelated compounds. (EX1009; Pet. 35-38.) Despite its complete lack of relevance, Petitioner argues that Talele teaches a skilled artisan to “substitute the ***methyl group*** on the 4-fluoro-1-methyl-indazole moiety of orforglipron ***with a cyclopropyl group***, thereby arriving at claimed Compound 19 of the ’236 Patent.” (Pet. 62 (emphasis added).)

Petitioner itself shows that Talele is cumulative by arguing that Yoshino and Kawai teach the same substitution. According to Petitioner, Yoshino discloses “several compounds wherein the methyl group of [orforglipron] is replaced by a ring structure” and suggests that “***replacement of the methyl group with a ring structure***

can preserve or restore the biological activity of the lead compound.” (Pet. 89, 92 (emphasis added).) Petitioner likewise argues that Kawai teaches that the GLP-1 receptor could “accommodate a bulkier hydrophobic substituent, such as a *three- to five-membered ring*, in place of the methyl group.” (Pet. 89 (emphasis added).) And, with those teachings in hand, a skilled artisan would purportedly know that “*cyclopropyl* represents the simplest and most structurally analogous to a methyl group, offering minimal steric deviation while providing favorable physicochemical properties consistent with the binding environment.” (Pet. 92.) Following its discussion of these cited references, Petitioner merely argues that Talele “further support[s]” the teachings of Yoshino, Kawai, and the knowledge of a skilled artisan, cementing its cumulateness. (*Id.*)

The Examiner was also well aware of the concept of cyclopropyl substitutions (the alleged teaching of Talele) during prosecution. Multiple references considered during prosecution disclosed cyclopropyl group substitutions on compounds with an orforglipron core. (EX2002, 360 (WO 2024/169,952 (“Huang”)), 525 (WO 2023/016,546), 588 (WO 2022/048,665), 648 (WO 2021/155,841).) Huang, for instance, cited in an IDS and appearing in the Examiner’s search report, discloses numerous such compounds. (EX2002, 360, 357, 438, 384.) The four following compounds include a cyclopropyl substitution (annotated in red) and were specifically identified in the Examiner’s search report:



(*Id.* (annotated).) Accordingly, Talele is also cumulative of Huang and other prior art of record generally disclosing the use of cyclopropyl rings.

Su.¹ Su published less than three weeks before the '236 patent issued, and thus was not considered during prosecution, but is substantially the same as other

¹ Petitioner submitted only a partial translation of Su, in violation of 37 C.F.R. § 42.63(b). (EX1031.) Ascleitis reserves the right to request that Su be excluded on

prior art considered by the Examiner. Petitioner cites Su to support its argument that a skilled artisan would make two changes to the structure of orforglipron to arrive at claimed Compound 19. (Pet. 3, 53, 55-56, 64.) More specifically, Petitioner argues that Su teaches (1) “replacing a methyl group on the indazole moiety with a cyclopropyl ring” and (2) “removal of methyl groups from the tetrahydropyran ring.” (Pet. 55, 30.)

These teachings were in front of the Examiner, as Petitioner’s own grounds make clear. In Ground 1, Petitioner asserts that Su, Yoshino, Kawai, and Talele render claimed Compound 19 obvious. (Pet. 46.) But in Ground 2, Petitioner alleges that Yoshino, Kawai, and Talele *without Su* also render Compound 19 obvious, meaning that Petitioner believes Su’s teachings are present in Yoshino, Kawai, and Talele, which as shown above were all considered during prosecution or are cumulative. This dooms Petitioner under *Advanced Bionics* Part 1. See *Parse Biosciences*, Paper 8 at 14 (where Petitioner “relie[d] on Saleh and Song in the

that basis. See *Toyota Motor North America, Inc. v. Cruise Control Techs. LLC*, IPR2014-00280, Paper 17 at 6 (PTAB July 2, 2014) (determining that a partial translation violates Rule 42.63(b) because Rule 42.63(b) requires "a translation of *the document* into English") (emphasis in original) (quoting 37 C.F.R. § 42.63(b) (2013)).

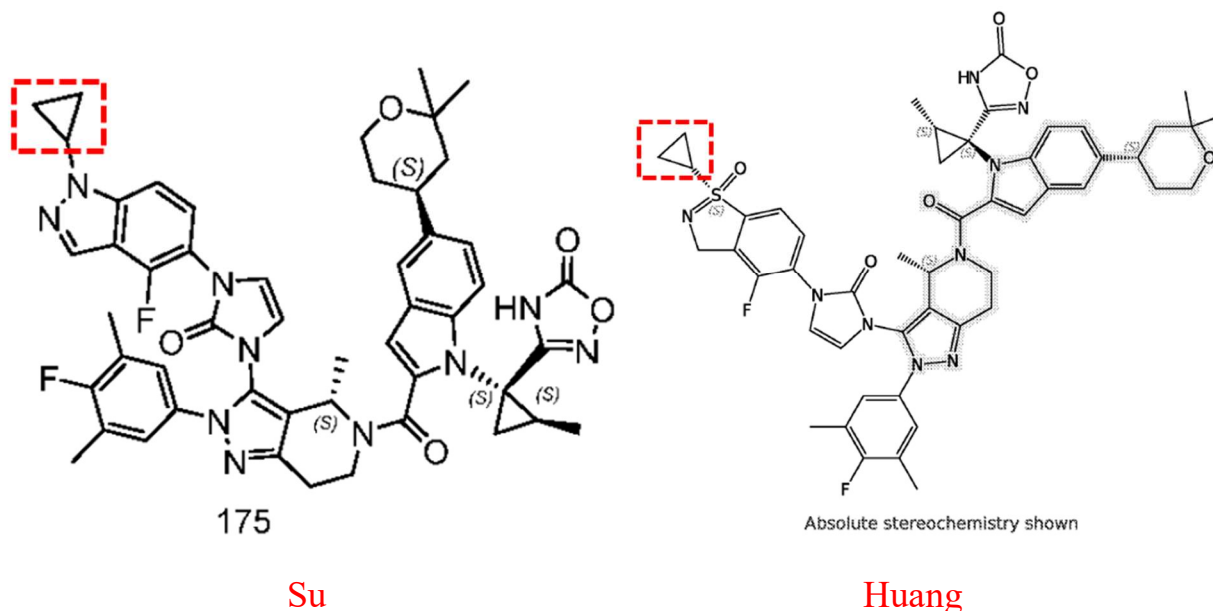
alternative for a similar teaching,” the Office determined that “Saleh is cumulative” of Song, which “was before the Examiner”); *Helena Labs. Corp. v. Sebia*, IPR2024-00801, Paper 10 at 12 (PTAB Oct. 23, 2024) (Office finding Huang reference cumulative where “Petitioner relies on both Shihabi and Huang as disclosing [the same teaching]” and Shihabi was considered during prosecution).

Petitioner’s arguments about the respective disclosures of Yoshino and Su further show that Su is cumulative. As shown below, Petitioner argues that both Yoshino and Su disclose the same modifications to the core structure of orforglipron.

Petitioner’s Arguments Based on Su	Substantially Similar Disclosure in Yoshino
“[T]he collective teachings of Su support a clear rationale for making the specific modifications embodied in Compounds 175 and 44, including <i>replacing a methyl group on the indazole moiety with a cyclopropyl ring</i> . . . (Pet. 55 (emphasis added), 30.)	“Yoshino, when considered as a whole, suggests to a POSA that <i>replacement of the methyl group with a ring structure</i> can preserve the biological activity of the lead compound.” (Pet. 23 (emphasis added), 92.) “Yoshino also teaches that <i>replacement of methyl with a ring</i> and removal of dimethyl results in improved or comparable activities as measured by EC50 values.” (Pet. 48 (emphasis added).) “Yoshino supports this conclusion by disclosing several compounds wherein the <i>methyl group of Compound 67 is replaced by a ring structure.</i>” (Pet. 89 (emphasis added).)
Su II teaches “<i>removal of methyl groups from the tetrahydropyran ring</i>	“Yoshino further teaches that modifications involving the <i>removal of</i>

Petitioner’s Arguments Based on Su	Substantially Similar Disclosure in Yoshino
in deuterated Compound 44, with its closest analog containing only hydrogen atoms in the tetrahydropyran ring (replacing D with H for at least simplified synthesis and removal of chiral center).” (Pet. 30 (emphasis added).) “[T]he collective teachings of Su support a clear rationale for making the specific modifications embodied in Compounds 175 and 44, including replacing a methyl group on the indazole moiety with a cyclopropyl ring . . . and <i>substituting a dimethyl-substituted tetrahydropyran ring with a non-substituted, achiral tetrahydropyran ring.</i>” (Pet. 55 (emphasis added).)	<i>methyl groups from the tetrahydro-2H-pyran moiety</i> generally do not compromise the biological activity of the compounds.” (Pet. 23 (emphasis added), <i>see also</i> 63.) “A POSA would understand that Yoshino expressly teaches that <i>removal of the dimethyl groups from the tetrahydropyran moiety</i> preserves, or even improves, biological activity.” (Pet. 96 (emphasis added).) “Accordingly, based on the disclosures of Yoshino and the structure-activity data therein, a POSA would have been motivated to <i>remove the dimethyl groups from the 2,2-dimethyl-tetrahydropyran moiety</i> of orforglipron.” (Pet. 97 (emphasis added).)
“Similarly, Su discloses GLP-1 receptor agonists and their pharmaceutically acceptable salts across multiple sections of the specification.” (Pet. 64.)	“Yoshino expressly discloses GLP-1 receptor agonists or salts thereof, including, for example, sodium and calcium salts.” (Pet. 64.)

Moreover, as explained above for Talele, other prior art before the Examiner also disclosed compounds with an orforglipron core and a cyclopropyl group substitution, like that relied on in Su. (EX2002, 360, 525, 588, 648.) Indeed, one compound in Huang has a cyclopropyl group in a similar location to Compound 175 of Su, which Petitioner relies on heavily:



(EX1006, 360; EX2002, 360 (annotated).)

Accordingly, Su is cumulative of Yoshino, Huang, and other prior art considered by the Examiner, and Petitioner's reliance on Su does not provide anything beyond what the Examiner already considered and rejected. Accordingly, the first prong of *Advanced Bionics* is met with respect to all the references relied on for Grounds 1 and 2.

b. The Petition Fails to Show that the Office Materially Erred in Considering the Art in Grounds 1 and 2

Petitioner has also failed to meet its burden to show that the Office materially erred in considering the prior art for Grounds 1 and 2. "If a condition in the first part of the framework is satisfied and the petitioner fails to make a showing of material error, the Director generally will exercise discretion not to institute [] review." *Advanced Bionics*, Paper 6 at 8-9. The *petitioner* bears the burden of establishing

that the examiner's error was significant and directly related to the patentability of the challenged claims. *Ecto World*, Paper 13 at 6 (“[I]f the Examiner applied the asserted prior art or substantially the same prior art during examination, then a petitioner must demonstrate that, for example, the previously presented art teaches the limitations of the challenged claims, and that no reasonable examiner could have found otherwise.”). Here, Petitioner makes two conclusory arguments on how the Examiner supposedly erred, but neither holds water.

First, Petitioner incorrectly argues that the Examiner failed to consider relevant prior art because the Notice of Allowance reproduces only a single exemplary prior art compound. (Pet. 119.) Petitioner reads far too much into the Notice of Allowance, which merely states that Yoshino “includes” that particular “exemplified compound.” (EX2002, 845.) From that innocuous statement, Petitioner makes the logical leap that the Examiner “failed to appreciate other compounds and disclosures in the prior art references.” (Pet. 119.) But there is no requirement that a Notice of Allowance include all the reasons why the claims were allowed; in fact, the MPEP instructs just the opposite. MPEP § 1302.14 (Notice of Allowance “not intended to necessarily state all the reasons for allowance or all the details why claims are allowed and ***should not be written*** to specifically or impliedly state that all the reasons for allowance are set forth.”) (emphasis added). Thus, the

Notice of Allowance in no way shows the Examiner failed to appreciate any prior art of record.²

Second, Petitioner is wrong that the Examiner “did not consider additional references, such as Su” because he “did not undertake any analysis to determine whether each of the claimed compounds are entitled to the earliest possible claimed priority date of the ’236 Patent.” (Pet. 119.) The MPEP does not require examiners to provide a priority analysis during the prosecution of every application. Instead, priority only becomes relevant when required for patentability reasons. MPEP § 216 (“The subject matter of the application is not examined to determine whether the

² That the Examiner pasted an image from the Examiner’s search report into the Notice of Allowance, instead of copying and pasting the same chemical structure from Yoshino is of no moment. There is no dispute that the image correctly depicts compound 77 from Yoshino. (*Compare* EX2002, 304, 763 with EX1008, 121.) If anything, the Examiner’s reproduction of the image from the search report shows the Examiner carefully reviewed that report, which includes nearly all of the compounds from Yoshino relied on in the Petition. (EX2002, 686 (Yoshino Compound 67), 788 (Yoshino Compound 40), 697 (Yoshino Compound 22), 721 (Yoshino Compound 64), 705 (Yoshino Compound 35), 701 (Yoshino compound 28), 707 (Yoshino Compound 38), 702 (Yoshino Compound 30).)

applicant is actually entitled to the priority of the foreign filing date unless such determination is required for patentability reasons.”). Here, there is no indication that the Examiner identified any references whose effect on patentability depended on the priority date. The only reference identified by Petitioner is Su, but the Examiner could not possibly have considered Su *itself*, regardless of any priority determination, because it was not even published yet when the Examiner allowed the claims. (EX1031 (showing publication date of February 6, 2025).) Thus, the lack of an explicit priority analysis also does not show the Examiner failed to consider any relevant prior art.

The Petition also fails to explain how the supposedly overlooked art would have led to a different outcome. *Google LLC v. Valtrus Innovations LTD*, IPR2022-01197, Paper 18 at 23 (PTAB June 13, 2023) (“[T]he express language of *Advanced Bionics* suggests that a petitioner should explain with specificity what it believes the previous error is and also show why that error is material to the patentability of the challenged claims.”). The Petition’s entire discussion of alleged material error spans a single page and does not explain how the allegedly overlooked references undermined the Office’s prior determination. (Pet. 119.) That alone prohibits a showing of material error. *Ecto World*, Paper 13 at 6 (“Petitioner’s generalized statements as to the strength of its Petition fail to identify sufficiently a material error.”).

Moreover, the Petition only identifies three specific disclosures that the Examiner supposedly “failed to appreciate”: (1) “Compound 67 of Yoshino,” (2) “the three-dimensional disclosures of Kawai that show the flexible and rigid regions of the compound,” and (3) Su. (Pet. 119.) But the Petition does not explain how those references would have changed the result during prosecution. (*Id.*) Indeed, Compound 67 of Yoshino is orforglipron, which is mentioned at least ninety-four times in the prosecution history and is used as a comparator in the specification of the ’236 patent itself. (EX1001, 104; *see, e.g.*, EX2002, 315, 439, 501, 871.) The idea that the Examiner did not consider that compound during prosecution is not believable. As to Kawai, it says nothing about potential modifications to orforglipron, leaving a skilled artisan with innumerable possibilities, even if Petitioner were correct that it teaches that the relevant GLP-1 binding pocket could accommodate an indazole moiety with “bulkier substituents.” (Pet. 119, 34-35.)

Nor would the Su reference have changed the outcome of prosecution. Petitioner’s argument that a skilled artisan would have started with Compound 175 of Su – out of over 200 disclosed compounds – is pure hindsight. In cherry-picking Compound 175, Petitioner fails to mention that that Su provides preclinical data for five compounds, ***none of which are Compound 175***. (EX1007, 294-95.) Clearly, a skilled artisan would have recognized that those five compounds, not Compound 175, were preferred in Su. Thus, if anything, Su teaches away from the claimed

invention. *Eli Lilly and Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, 1379 (Fed. Cir. 2006) (finding “the prior art taught way from selecting Compound ’222 as a lead compound for further development” where “the primary example of the state of the art at that time, the ’574 patent, did not provide any biological data for compound ’222”).

Moreover, far from supporting obviousness, Su instead shows large number of unpredictable options available to a skilled artisan trying to modify the core orforglipron structure. Su alone includes many modifications to the orforglipron core structure, which can be mixed and matched, leading to a very large number of potential compounds, and does not disclose any way to predict the results. Su, thus, does nothing to make the challenged claims obvious. *Ortho-McNeil Pharms. Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1363-65 (Fed. Cir. 2008) (finding defendant has not shown obviousness where “this clearly is not the easily traversed, small and finite number of alternatives that *KSR* suggested might support an inference of obviousness”).

The Office, in fact, has already reached the same conclusion. Related U.S. Patent No. 12,291,530 claims compounds with a similar core structure to those claimed in the ’236 patent and *a cyclopropyl substitution on the indazole moiety*. (EX2006, 53-56.) During the prosecution of that patent, after the examiner had already allowed the pending claims, Ascletis submitted an IDS citing the recently-

published Su reference. (EX2003, 514.) After considering Su (EX2003, 545), the examiner issued a Corrected Notice of Allowability, finding the claims allowable because “[t]he new reference provided in the IDS does not result in reopening the prosecution as there is no teaching or suggestion that would motivate one skilled in the art to modify the compounds to achieve the claimed invention, justifying the allowance of the claims.” (EX2003, 549.)

Finally, Petitioner’s own patent application – which it failed to tell the Office about in the Petition – contradicts its argument that the Examiner erred. On December 22, 2023, three months *after* the earliest priority date for the ’236 patent, CSPC filed a Chinese provisional application related to GLP-1 agonists that later published as WO 2025/131,043. (EX2005, 1.) The PCT publication discloses and *individually claims* Compound 1, one of the compounds that Petitioner now says would have been obvious as of an even earlier priority date. (EX2005, 95-96 (Compound 10 of Claim 10).) Petitioner’s obviousness arguments, made only after it learned that Ascletis invented and filed first on these compounds, cannot be squared with CSPC’s patent application. *See Anderson Corp. v. Pella Corp.*, 300 F. App’x 893, 899-900 (Fed. Cir. 2008) (finding that the accused infringer’s later patent applications to similar subject matter weighed against a finding of obviousness).

Given that the art in Grounds 1 and 2 was considered during examination and the Examiner did not overlook or misapprehend any prior art teachings, Petitioner’s

allegations of material error do not clearly and convincingly demonstrate that the Office erred in a manner material to patentability.

2. Ground 3 Fails the *Advanced Bionics* Framework

Ground 3 depends on the success of Ground 1 or 2. (Pet. 105-06 (“Compound 65 differs from Compound 19, addressed *supra* in Grounds 1 and 2, by the incorporation of a nitrogen atom into the aromatic ring to which the tetrahydropyran moiety is attached, as illustrated below. As detailed in Grounds 1 and 2, a POSA would have found it obvious to arrive at Compound 19 based on the combined teachings of Su, Yoshino, Kawai, and Talele.”).) Petitioner cites additional prior art in Ground 3 (Meng, Ren, Patel)³ solely to try to show the incorporation of the nitrogen atom into the aromatic ring of Compound 65 would have been obvious

³ The Petition does not clearly articulate what references support Ground 3. The Petition’s Identification of Challenge section states that Ground 3 includes the Ground 1 references plus *Meng, Patel and Ren*. (Pet. 7 (emphasis added).) But, later for in the Ground 3 section, the Petition identifies “the combination of Su, Yoshino, and Kawai, further in view of Talele, *Patel, and Pennington*.” (Pet. 105 (emphasis added).) Despite the lack of clarify, Ascleitis addresses all of these references in this brief, but does not concede Ground 3 was properly plead or waive any rights to object to Ground 3.

starting from Compound 19. (Pet. 106-12.) Thus, if the Office agrees with Ascleitis that discretionary denial is appropriate for Grounds 1 and 2, it also must be appropriate for Ground 3, as the additional references could not possibly have changed the outcome during prosecution. *See Motorola Mobility LLC v. Maxell, LTD.*, IPR2022-01287, Paper 11 at 21-22 (PTAB Feb. 2, 2023) (concluding that the references “relied upon only in combination with [the primary reference] for teaching limitations of the dependent claims” are cumulative to the primary reference).

Regardless, the additional references were considered during prosecution or are cumulative. The inventors disclosed Meng in an IDS, and the Examiner indicated the reference was considered. (EX2002, 274, 867.) Likewise, Ren was identified in the Examiner’s search report. (EX2002, 478-96.) Finally, Patel and Pennington are generic references that discuss nitrogen substitution in aromatic rings and do not relate orforglipron or to GLP-1 agonists. (Pet. 108-09.) They are both cumulative of Meng and Ren, and Petitioner offers no analysis to the contrary. *Parse Biosciences*, Paper 8 at 14; *Alarm.com*, Paper 6 at 20. Finally, the Petition provides no argument for Examiner error based specifically on Meng, Ren, Patel, or Pennington. (Pet. 116-19.)

Accordingly, discretionary denial is also appropriate for Ground 3.

3. Ground 4 Fails the *Advanced Bionics* Framework

Ground 4 challenges only claims 4 and 9 and relies on Su and Bethel. (Pet. 115-16.) Claims 4 and 9 each depend from claim 1 and require a hemicalcium salt of one or more of the compounds of claim 1. Petitioner alleges that Su teaches one or more of the claimed compounds, and Bethel teaches hemicalcium salts of orforglipron. (*Id.*)

For the same reasons previously discussed, Su is cumulative of prior art that was before the Examiner, including Yoshino and Huang, and Petitioner has not established that the Examiner erred in considering that art. (*See supra* Section II.A.1.a.)

Bethel was considered during prosecution. The patentees disclosed Bethel in an IDS, and the Examiner considered Bethel. (EX2002, 865.) Bethel was also one of the references that resulted from the Examiner's search. (EX2002, 472.) As a result, Prong 1 of the Advanced Bionics framework is satisfied as to Bethel. *See, e.g., Ecto World*, Paper 13 at 4; *Keysight Techs.*, Paper 14 at 5.

Petitioner has also failed to demonstrate that the Examiner erred in considering Bethel. Initially, the Petition provides no argument for Examiner error based on the combination of Su and Bethel. (Pet. 116-19.) Indeed, the Petition's cursory discretionary denial section does not even mention Bethel. (*Id.*) And the Petition only argues that the Examiner "failed to identify" Su but provides no

explanation how Su would have changed the result during prosecution for any claim, much less the two specific claims challenged in Ground 4. (Pet. 119.) This fact, by itself, precludes any determination of Examiner error. *Ecto World*, Paper 13 at 6.

The Examiner was also justified in allowing claims 4 and 9 over Bethel. Bethel discloses hemicalcium salts of a different compound, orforglipron, not any of the compounds claimed in claims 4 and 9. (EX1032, 18.) As the Federal Circuit has found before, it is impossible to know in advance if any individual compound will form a salt with a particular counterion. *Pfizer Inc. v. Apotex, Inc.*, 480 F.3d 1348 at 1364 (Fed. Cir. 2007) (accepting the district court’s finding that “it was generally unpredictable as to whether a particular salt would form and what its exact properties would be”).

Discretionary denial is also appropriate for Ground 4.

III. CONCLUSION

For the foregoing reasons, Ascleitis respectfully requests that the Office exercise its discretion to deny institution under 35 U.S.C. § 325(d).

Dated: September 8, 2025

Respectfully submitted,

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CERTIFICATE OF WORD COUNT (37 C.F.R. § 42.24(d))

1. This Patent Owner's Brief In Support of Discretionary Denial complies with the type-volume limitation of 14,000 words, comprising 5,258 words, excluding the parts exempted by 37 C.F.R. § 42.24(a)(1).

2. This Patent Owner's Brief In Support of Discretionary Denial complies with the general format requirements of 37 C.F.R. § 42.6(a) and has been prepared using Microsoft® Word 2016 in 14-point Times New Roman font.

Dated: September 8, 2025

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CERTIFICATION OF SERVICE UNDER 37 C.F.R. §§ 42.6(e), 42.105(a))

I, W. Chad Shear, hereby certify that on this 8th day of September 2025, the foregoing **PATENT OWNER'S BRIEF IN SUPPORT OF DISCRETIONARY DENIAL** was served electronically via email on the following:

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