

Filed: December 26, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEUROCRINE BIOSCIENCES, INC.
Petitioner,

v.

SPRUCE BIOSCIENCES, INC.,
Patent Owner.

PGR2022-00025
Patent 11,007,201 B2

**PATENT OWNER SPRUCE BIOSCIENCES, INC.'S
REQUEST FOR DIRECTOR REVIEW PURSUANT TO 37 C.F.R. §42.75**

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I. PRECISE RELIEF REQUESTED

Spruce respectfully requests that the next Presidentially-appointed USPTO Director vacate the final written decision (FWD) and the interlocutory decisions rendered in reaching that decision (including Papers 13, 15, 20), deny institution, and terminate this proceeding. 37 C.F.R. §42.75(a). As explained below, these decisions present (a) abuse of discretion, (b) raise important issues of law or policy, (c) erroneous findings of material fact (including omission of numerous undisputed material facts), and (d) rest on erroneous conclusions of law.

II. PROCEDURAL HISTORY

This case is a follow-on case Petitioner filed against a continuation patent after its challenge against Patent No. 10,849,908 failed. On December 10, 2021, the PTAB denied the petition in PGR2021-00088 challenging the '908 Patent because Petitioner's self-defeating admissions demonstrated it failed to satisfy its burden of proof. PGR2021-00088 Paper 11, 2.

In relevant part, the PTAB rejected Petitioner's argument that the method claims—using admittedly-known about “100 compounds” that make up “CRF1 receptor antagonists”—lacked adequate written description support because the specification's actual reduction to practice was clinical data obtained with a particular CRF1 receptor antagonist, tildacerfont. PGR2021-00088 Paper 11, 26-30. In particular, the PTAB found Petitioner's own prior art and expert

acknowledged the genus “was well known in the art at the time of the invention,” and the specification discloses “the genus was well known in the art, identifies an example, and provides an exemplary embodiment in which it is administered to achieve the claimed effect.” *Id.*, 26-30. The PTAB also rejected the enablement challenge, finding a lack of argument/evidence of “undue experimentation,” that Petitioner’s declarant “testifies that the genus of CRF1 receptor antagonists was known in the art,” and disclosure of “mechanism of action, a working example, and clinical protocols used to verify efficacy.” *Id.*, 33-34.

Within months, Petitioner filed a Request for Precedential Opinion Panel (POP) Rehearing (PGR2021-00088 Paper 12) and then attacked the continuation ’201 Patent with a follow-on Petition in PGR2022-00025. But both of Petitioner’s procedural maneuvers failed to identify anything the PTAB had overlooked. In the rehearing request, Petitioner accepted that CRF1 receptor antagonists were a well-known class, but argued the specification provides only a single CRF1 receptor antagonist working example. PGR2021-00088 Paper 12, 2. Spruce was never authorized to provide any response. Nov. 2019 PTAB Trial Practice Guide 90 (No response allowed “absent a request from the Board.”).

In the second Petition, Petitioner altered its expert’s testimony to excise the damning admissions he provided in his first declaration, hoping the PTAB wouldn’t notice. Paper 27, 72-73 (POR noting admission eliminated from

PGR2022-00025 EX1005, ¶96). Instead, the PTAB held Petitioner accountable and found that the second petition did not remedy the deficiencies of the first. Paper 10, 33-34 (citing PGR2021-00088 Paper 11) (“We addressed Petitioner’s same argument for lack of written description support in PGR2021-00088. Petitioner has not addressed these previous findings or why these findings are in error.” PGR2022-00025 Paper 10, 33-34 (citations omitted). Petitioner repeated its meritless rehearing requests one more time. Paper 11, 5.

Over 18 months after the PTAB soundly rejected Petitioner’s arguments the first time, then-USPTO Director Vidal eliminated the POP and *sua sponte* ordered Director Review of the institution denial. Papers 13-14 (July 20, 2023). Director Vidal cited interim process provisions created well after Petitioner’s request was filed, did not identify what issue(s) she would consider, and did not authorize Spruce to respond to her order or to Petitioner’s rehearing arguments. Paper 13, 2. Director Vidal then vacated the institution decision and remanded for further proceedings. Paper 15 (Aug. 4, 2023).

Regarding written description, Director Vidal did not disturb the PTAB’s finding that the specification describes a method for treating CAH by administering a CRF1 receptor antagonist, discloses the genus was well known in the art, identifies an example, and provides an exemplary embodiment in which it is administered to achieve the claimed effect, or that Petitioner’s own prior art and

expert acknowledged that the genus was well known in the art at the time of the invention. Paper 15, 2-3 (incorporating reasoning from PGR2021-00088 Paper 16 (*see* 3-4, 10-14)). Director Vidal discussed a need for identification of structural features common to the members of the genus. PGR2021-00088 Paper 16, 12. Director Vidal also stated that even where the class is already known, as acknowledged here, written description requires disclosure of a method sufficient to distinguish CRF1 receptor antagonists that satisfied the functional requirements of the claim from those that might not. *Id.*, 13, 14. Ultimately, Director Vidal remanded to the PTAB with this instruction: “Description of a single compound in the genus or knowledge generally of the genus’ members, without more, is insufficient to demonstrate possession of such broad method claims.” *Id.*, 14.

The PTAB instituted review (Paper 20, Dec. 1, 2023) and the remand panel followed the Director’s instructions, reasoning that she had already concluded the specification “does not disclose a representative number of species” or “structural features common to the members of the functional genus[.]” Paper 20, 32.

On November 27, 2024, more than 3.5 years after the first Petition was filed, the remand panel declared all challenged claims unpatentable for lack of written description, without accepting any of the Petition’s other arguments. Paper 62 (Nov. 27, 2024). The FWD did not recant the PTAB’s finding that the specification describes a method for treating CAH by administering a CRF1 receptor antagonist,

discloses that the genus was well known in the art, identifies an example, and provides an exemplary embodiment which is administered to achieve the claimed effect, or that Petitioner's own prior art and expert acknowledged that the genus was well known in the art at the time of the invention. Nor did the FWD recant that the specification discloses the mechanism of action, a working example, and clinical trial protocols used to verify efficacy (i.e., a method of distinguishing effective from ineffective compounds).

Nor could the remand panel recant these facts; none of them were disputed between the parties. Petitioner and its expert confirmed at trial that CRF1 inhibitors were a known class of about 100 compounds, those compounds had already been structurally characterized in published literature with identification of structure common to members of the class (including Petitioner's own peer reviewed publication), and that the art had already described class-wide therapeutic efficacy for CAH. Paper 10, 33-34; Paper 27, 66-78; Paper 43, 17-24; *see also* EX2010, ¶¶23-24, 99; EX1047, ¶¶23, 83. That is not all. Petitioner's expert also agreed that the challenged patents' 14-day protocol was a "method of distinguishing effective from ineffective compounds" and that *Petitioner* had published a study using the same protocol, which was post-filing evidence corroborating descriptive support in the challenged patents. Paper 43, 21-22; EX2027, 18:10-21:5, 75:21-76:14; *see also* Paper 27, 33-35, 67-71; EX2014, ¶¶41, 78-79. The FWD largely ignored these

aspects of Petitioner's self-defeating case.

III. LEGAL STANDARDS

Pursuant to 37 C.F.R. § 42.75(a)-(b), a party may request Director Review of any final decision under 35 U.S.C. §328 as well as “any interlocutory decision rendered by the Board in reaching that decision.”

IV. ARGUMENT

A. *Director Vidal Denied Spruce Due Process by Granting Sua Sponte Director Review and Vacating the PTAB Decision Without Affording Spruce with Notice and an Opportunity to Respond.*

The USPTO, the PTAB, and the USPTO Director are all required by the U.S. Constitution and by federal statute (e.g., Administrative Procedure Act) to afford every patent owner due process in any proceeding that can result in deprivation of the patent owner's property. Fifth Amendment, U.S. Constitution; 5 U.S.C. §554(b)-(c). Therefore, no government action adverse to the patent owner is permitted without *first* providing the patent owner with timely notice of the nature of the hearing (e.g., the specific issue(s) to be decided and the arguments and evidence therefor) *and* an opportunity to be heard. More particularly, any time a federal agency reviews the decision of subordinate employees, “the parties are entitled to a reasonable opportunity to submit for the consideration of the employees participating in the decisions—(1) proposed findings and conclusions.” 5 U.S.C. §557(c). The appropriate remedy for a deprivation of due process is to

vacate the agency decision that was issued without affording the patent owner appropriate notice **and** opportunity to be heard. *In re NuVasive, Inc.*, 841 F.3d 966, 967-968 (Fed. Cir. 2016).

Here, Director Vidal doubly denied Spruce's Due Process right. First, Director Vidal *sua sponte* granted Director Review without first providing Spruce with **any notice** that the PTAB's decision was under consideration for Director Review or of the issue(s) that might merit Director Review. Paper 13. If Director Vidal believed Petitioner's rehearing and POP request had any merit, the Director had more than **eighteen months** to inform Spruce and to provide Spruce with an opportunity to respond. PGR2021-00088 Paper 11 (Dec. 10, 2021 first decision denying institution); PGR2022-00025 Paper 13 (July 20, 2023). Instead, Director Vidal provided Spruce with no notice or opportunity to respond before deciding to initiate Director Review adverse to Spruce's property interests.

Within two weeks, Director Vidal had already published her decision on Director Review. Paper 15 (Aug. 4, 2023). Director Vidal thereby compounded her first Due Process violation by vacating the PTAB's non-institution decision without first advising Spruce of the issue(s) of concern to the Director **and** providing Spruce with an opportunity to respond. The order granting *sua sponte* Director Review was silent as to what issue(s) prompted the order, did not authorize any response, and instead stated that "I will issue an order or decision in

due course.” Paper 13. But no scheduling order or decision identifying for briefing the issues on review ever issued. Instead, Spruce was first informed of the scope of the jurisdiction Director Vidal had elected to exercise and the matters of fact and law asserted by the Director when Director Vidal issued her decision (Paper 15) vacating the institution denial just two weeks later. After eighteen months of repose since the first challenge failed, with two valid decisions explaining why Petitioner’s challenges were meritless, Director Vidal completely flipped the outcome within two weeks without ever identifying the issue(s) under consideration or affording Spruce any opportunity to respond. These were egregious violations of Spruce’s Due Process rights.

B. *Director Vidal’s Due Process Violations Infected the FWD Prejudicially to Spruce’s Rights in its Patent Property.*

Due Process violations are pernicious exactly because of the arbitrariness, unfairness, and capriciousness of reaching a pre-determined outcome before hearing from the adversely-affected party. *See* 5 U.S.C. §706(2)(A)-(D). Here, there can be no dispute that Director Vidal’s mind was made up while Spruce never even was advised what was of concern to her or had any chance to respond.

Director Vidal’s deprivation of Spruce’s Due Process rights altered and affected the PTAB panel to Spruce’s material prejudice. The PTAB instituted the proceeding (Paper 20, Dec. 1, 2023). Regarding written description, the remand institution decision reasoned that Director Vidal already had concluded the

specification “does not disclose a representative number of species” and “does not disclose structural features common to the members of the functional genus so that one of skill in the art can visualize or recognize the effective members of the genus[.]” Paper 20, 32; *see also* Paper 15, 2-3, PGR2021-00088 Paper 16, 12-13. During trial, Spruce explained that the two written description issues identified by Director Vidal had been resolved in Spruce’s favor. First, it was undisputed that common structures had been identified. Paper 27 (POR), 71-78; Paper 43 (PO Sur-Reply), 19-21, 22-24; *see also* EX1029, 2, Fig. 2; EX1018, 3, Fig. 1; EX2014, ¶¶83-84. Second, it was undisputed that the specification disclosed a method to recognize effective members of the genus. Paper 43 (PO Sur-Reply), 21-22; EX2027, 18:10-21:5, 75:21-76:14. Due Process violations were thus compounded by the panel largely ignoring facts resolved at trial in Spruce’s favor and instead treating the Director’s *sua sponte* intervention as an outcome-oriented directive.

Perceiving Director Vidal (Paper 15, 2-3) as adopting a *per se* rule requiring more than one working example for written description of claims to using a genus of structurally-diverse receptor antagonists, the remand panel impermissibly adopted a pre-determined outcome for written description. The panel therefore never reconciled its conclusion of no written description with its undisputed and undisturbed findings from the first challenge that the specification discloses a “mechanism of action, a working example, and clinical trial *protocols used to*

verify efficacy.” Paper 20, 32; PGR2021-00088 Paper 21, 46, 49; *but see*

PGR2021-00088 Paper 16, 13 (recognizing written description would be provided if the specification provides a “method of distinguishing effective from ineffective compounds” (citing *Idenix Pharmaceuticals LLC v. Gilead Sciences Inc.*, 941 F.3d 1149, 1164 (Fed. Cir. 2019))).

The prejudice imposed via the remand panel by Director Vidal became known to Spruce more than 3.5 years after the first Petition was filed when the remand panel declared all challenged claims unpatentable for lack of written description. Paper 62 (Nov. 27, 2024). The FWD did not recant the PTAB’s finding that the specification describes a method for treating CAH by administering a CRF1 receptor antagonist, discloses that the genus was well known in the art, identifies an example, and provides an exemplary embodiment which is administered to achieve the claimed effect, or that Petitioner’s own prior art and expert acknowledged that the genus was well known in the art at the time of the invention. Paper 10, 5, 33-34; PGR2021-00088 Paper 11, 3, 26-30. Nor did the FWD recant that the specification discloses the mechanism of action, a working example, and clinical trial protocols used to verify efficacy (i.e., a method of distinguishing effective from ineffective compounds). Paper 10, 33-34; PGR2021-00088 Paper 11, 28-30, 33-34. The PTAB panels authorized to decide whether to institute the Petitions had decided in December 2021 and September 2022 that the

Petitioner had failed to satisfy its burden of proof on these sound bases. Because these facts were (and are) undisputed, the specification indisputably provided written description support for the claims. Petitioner's requests for rehearing and POP review did not challenge any of these material, dispositive facts. Papers 11-12. If Spruce had been afforded an opportunity to respond before Director Vidal intervened and reached her final conclusion, Spruce would have explained that any alleged errors in the PTAB's decision denying institution were non-prejudicial and at most constituted harmless error in view of the undisputed evidence.

The failure of the remand panel's FWD to address material and even undisputed evidence supporting written description confirms that Director Vidal's repeated deprivation of Spruce's Due Process rights resulted in material prejudice against Spruce. For example, undisputed evidence established that the patent specification described how to distinguish claimed from unclaimed subject matter (Paper 27, 67-71; Paper 43, 21-22; *see also* EX1001, 33:52-59 (capsule content), 41:43-42:47 (dosing protocols), 43:34-53 & Figs. 2-4 (hormone level reductions); EX2014, ¶78). The remand panel ignored evidence of class-wide efficacy. Paper, 27, 79-80, 78; Paper 43, 22-24; *see also* EX1001, 10:61-65, 12:26-29. The remand panel also ignored the failure of the Petition to even argue, let alone provide any evidence of, unpredictability when using the method in the specification. Indeed, the remand panel ignored that Petitioner commissioned its own study repeating the

method from the challenged patent for a second CRF1 receptor antagonist, further corroborating the adequacy of the written description support in the specification.

Paper 43, 21-22; *see also* EX1009; EX2027, 18:10-21:5 (Neurocrine's expert testifying the 14-day oral dosing protocol was clearly able to identify whether a CRF1 receptor antagonist reduces hormone levels from baseline as required by the claims), 75:21-76:14, 158:10-15 (A4 levels). The remand panel overlooked this evidence entirely and never addressed it. By this time, Director Vidal's complete deprivation of Spruce's Due Process rights had prejudiced the panel into believing that the outcome (cancelling of Spruce's claims under written description) was pre-ordained by the Director regardless of what the evidence showed.

Rather than address the salient, material, and undisputed record at trial, the FWD relied on a new argument never presented during trial. In particular, FWD spends several pages discussing peptide antagonists of CRF1 that the decision says were disregarded in the art in favor of small molecule antagonists because of obstacles to employing peptides due to the blood brain barrier. Paper 62, 45, 54-55. Notably, the remand panel's discussion of peptide antagonists never cites the Petition or any other paper from either party because *none of this was argued by the parties*. Indeed, both parties had proceeded under the understanding that the claims were directed to small molecule CRF1 receptor antagonists, the well-known class identified in the Petition and admitted by Petitioner's expert.

Whereas the FWD adopted a new argument that the specification's complete absence of discussion of peptides should be interpreted to expand the claims to cover them (Paper 62, 54-55), the decision denying institution had recognized what both parties maintained throughout the proceeding—the claims were directed to the known class of small-molecule CRF1 receptor antagonists. Paper 10, 33 (“the genus of CRF1 receptor antagonists was well known in the art at the time of invention” and Petitioner’s declarant “acknowledges that this genus would have been well known to a person of ordinary skill in the art”); *see also* PGR2021-00088 Paper 11, 31-32 (recounting specification’s “description of the development of ‘biologically-active small molecules having significant CRF receptor binding activity and which are capable of antagonizing the CRF1 receptor’ to reduce ACTH levels by reducing CRF secretion.”). Though the remand panel authorized post-hearing briefing to address a discrete claim construction issue, it never authorized briefing on this new peptide argument it adopted in the FWD. Paper 56.

The prejudice to Spruce resulting from Director Vidal’s Due Process violations were exacerbated by the remand panel’s failure to abide by the conditions of replacing Petitioner’s original expert. Paper 62, 6-7, 14-16. The substitute expert was bound by the original expert’s testimony, which included his admission relied upon repeatedly by the PTAB that the class at issue was identifiable as “over 100 compounds” and was “well known in the art at the time of

invention.” E.g., Paper 10, 33-34; PGR2021-00088 Paper 11, 26, 29. This testimony was adopted by Petitioner’s substitute expert and was never recanted. Paper 43, 19-20; EX1041, ¶¶15-16; EX2027, 112:15-17; Paper 62, 16-17 (“Dr. Cutler’s Declaration appropriately adopts the Carey Declaration in full and makes no additional substantial argument with respect to the merits of the case.”). But somehow, the remand panel ignored that admission and relied instead on an “indeterminate number of unique chemical structures” argument that finds no place in the Petition materials. Paper 62, 55. Such departures from the Petition case are squarely forbidden. *SAS Inst., Inc. v. Iancu*, 584 U.S. 357, 366-67 (2018).

The remand panel’s decision to raise and adopt new arguments without notice and opportunity to be heard can only be viewed as a prejudicial result of Director Vidal’s repeated deprivations of Spruce’s Due Process rights. In other words, without notice to Spruce, Director Vidal made it clear to the remand panel that it was “open season” on Spruce’s patent property rights without Due Process, and this violation manifested against Spruce prejudicially in the FWD. Accordingly, the proper remedy is to vacate the FWD, as well as all interlocutory decision rendered in reaching that decision (including Papers 13, 15, and 20).

C. *Dr. Carey Was Never an Available Witness.*

As a housecleaning matter, Spruce filed a motion requesting record clarification that Petitioner has only one supporting witness, not two, by excluding

the duplicate version of the Carey Declaration. Paper 62, 14-15. The FWD denied the motion on the basis that there was no “evidence that inclusion of the Carey Declaration colorably prejudices its case” because any “risks [of] the prejudicial false impression” of two witnesses “have no merit.” *Id.*, 16. Yet, on the very same page, the remand panel itself confuses witnesses and creates “the prejudicial false impression Petitioner has two supporting witnesses” by incorrectly declaring Spruce “deposed Dr. Carey [the withdrawn expert] twice.” *Id.*, 16. Dr. Carey was never deposed—he was “medically incapacitated and incapable of testifying at deposition.” *Id.*, 15-16.

V. CONCLUSION

Because of the repeated abuses of Spruce’s Due Process rights stretching over a period approaching four years, the appropriate remedy is for the next Presidentially-appointed USPTO Director to vacate the FWD (Paper 62) and the interlocutory decision rendered in reaching that decision (including Papers 13, 15, and 20), and issue a decision denying institution and terminating the proceeding. As the history of this proceeding shows, no subordinate employee will depart from Director Vidal’s arbitrary and prejudicial actions in this case.

Respectfully submitted,

Dated: December 26, 2024

/Michael T. Rosato/
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CERTIFICATE OF SERVICE

This is to certify that I caused to be served a true and correct copy of the foregoing Patent Owner Spruce Bioscience, Inc.'s Request for Director Review pursuant to 37 C.F.R. § 42.75, on this 26th day of December, 2024, on the Petitioner at the correspondence address of record as follows:

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Respectfully submitted,

Dated: December 26, 2024

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