UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEUROCRINE BIOSCIENCES, INC.,
Petitioner,

v.

SPRUCE BIOSCIENCES, INC.,
Patent Owner.

Case No. PGR2026-00060
Patent No. 12,569,490 B2

PATENT OWNER'S BRIEF IN SUPPORT OF DISCRETIONARY DENIAL

TABLE OF CONTENTS

I. Introduction....1

II. Neurocrine's Harassment Warrants Discretionary Denial....2

A. Court Records Document Petitioner's Litigation Abuse. 3

B. Petitioner's Wasteful Harassment is Already Widespread. 5

III. The Challenged Claims Cured any Perceived Defects from Neurocrine's Prior PGR Challenges....5

A. The Challenged Claims Cure the Perceived Defect of the Prior PGR Decisions. 6

1. The Present Claims Are Materially Different.....6

2. The Examiner Fully Considered Petitioner's Challenges Before Issuing the Present Claims. 7

B. Allowance of New Claims Under Scrutiny Arising from Petitioner's Prior PGRs Gave Rise to Strong Settled Expectations. 8

IV. Petitioner's Present Challenge Should be Rejected Under 35 U.S.C. §325(d) As Cumulative and Wasteful. 12

A. The Office Already Considered Section 112 During Prosecution.....13

B. No Demonstration of Material Error....14

V. Conclusion 15

VI. Appendix....17

I. INTRODUCTION

Spruce Biosciences, Inc. is a small American company dedicated to advancing targeted, first-in-class therapies that address serious, underserved neurological conditions. For years now, Neurocrine Biosciences, Inc. ("Petitioner") has been aggressively courting Spruce, demanding unpaid access to Spruce's technology. Petitioner vowed to "initiate legal and administrative proceedings" to exploit Spruce's "cash burn rate" until Spruce would give in to its demands. This is all documented in Petitioner's failed district court action (EX2001-EX2002), which Petitioner omits here. Now, Petitioner's PGR Nos. 2026-00059, 2026-00060, and 2026-00061 are just the latest salvo in Petitioner's improper harassment campaign against Spruce. But the use of AIA reviews as a harassment tool, as here, is contrary to Congress's intent, and is wasteful. Accordingly, these petitions should be discretionarily denied.

Underscoring concerns of improper harassment, Petitioner asks the Board here to rehash the same issues addressed during prosecution without identifying any material error. Petitioner argues that the claims lack written description because the PTAB previously found that different, much broader claims lacked written description. But the present claims are not only materially different, they were purposefully narrowed to a handful of specific compounds expressly identified in the specification to address the breadth concerns previously raised by

the PTAB. Indeed, the Office issued the presently challenged claims with full knowledge of the PTAB's prior decisions. Accordingly, Spruce respectfully asks the Director to reject Petitioner's request for institution.

II. NEUROCRINE'S HARASSMENT WARRANTS DISCRETIONARY DENIAL

This case presents a textbook example of a petitioner trying to misuse Office resources for harassment, market advantage, and for the petitioner's financial benefit. Petitioner has expressly proclaimed it would "initiate legal and administrative proceedings," and exploit Spruce's "cash burn rate" to extort its demanded royalty-free access to Spruce's intellectual property portfolio. All of this is documented in Petitioner's failed district court action (e.g., EX2001-EX2002), which Petitioner conspicuously omits from its petition materials.

This is precisely the type of abuse of AIA proceedings the Director has identified as a waste of Office resources, warranting discretionary denial. *See, e.g.*, *Magnolia Medical Techs., Inc. v. Kurin, Inc.*, IPR2026-00097, Paper 17 (May 14, 2026) (precedential) ("Congress was clear that AIA reviews should not be used 'for harassment or a means to prevent market entry through repeated litigation and administrative attacks'" (quoting H.R. Rep. No. 112-98 at 48 (2011))); *OpenSky Industries, LLC v. VLSI Technology LLC*, IPR2021-01064 Paper 102, 28-29 (Oct. 4, 2022) (precedential) (Congress never intended AIA proceedings "to be tools of patent owner harassment" and the Office has been clear that such "[a]buse of AIA

proceedings undermines the[] important objectives" of the AIA); *Patent Quality Assurance, LLC v. VLSI Technology LLC*, IPR2021-01229 Paper 102 at 39 (Dec. 22, 2022) ("AIA proceedings were not, however, intended…to be tools of patent owner harassment."); *see also WesternGeco LLC v. ION Geophysical Corp.*, 889 F.3d 1308, 1317 (Fed. Cir. 2018) ("Congress recognized the importance of protecting patent owners from patent challengers who could use the new administrative review procedures as 'tools for harassment.'").

A. Court Records Document Petitioner's Litigation Abuse.

Petitioner's stated objective to misuse litigation and administrative attacks for market advantage and financial gain has been clear and well-documented. In December 2024, counsel for Petitioner demanded from Spruce a broad "covenant not to sue Neurocrine (and its licensees) on ***any*** of its U.S. patents and their foreign counterparts (now and in the future) with claims directed to ***CRF_1 receptor antagonists***, including crinecerfont." EX2003. In follow-on letters, Petitioner clarified that it wanted nothing less than "unconditional" access to Spruce's intellectual property portfolio that must be given "without charge." EX2004.

To force compliance, Petitioner expressly threatened to bring the very "administrative proceedings" advanced here if Spruce did not satisfy Petitioner's demands. EX2005 ("Neurocrine will initiate legal and administrative proceedings, both in the U.S. and elsewhere"). Petitioner characterized its repeated litigation

attacks as designed to exploit what it considered to be Petitioner's financial superiority and Spruce's "cash" vulnerability. Petitioner taunted Spruce as being in "desperate need for cash," which it said left Spruce with only "a one-year runway based on its current cash burn rate." EX2006, 4; *id.*, 10, 20 ("desperate need for cash (with a one-year runway based on its current cash burn rate)"). Thus, Petitioner itself has openly acknowledged its repeated litigation and administrative attacks on Spruce's patent portfolio are a tool to harass Spruce.

One district court, however, already rejected Petitioner's litigation as an artificially "manufactured" harassment campaign to extract a cost-free license to Spruce's portfolio. EX2002, 1. Petitioner brought suit in the District of Delaware against Spruce's U.S. Patent No. 11,344,557 on the basis that Spruce "repeatedly refused to provide Neurocrine with a covenant not to sue for infringement of the Spruce CAH patents, or to refrain from challenging the FWDs invalidating the '908 and '201 patents." EX2006, 3. Spruce explained that Petitioner was misusing legal proceedings to extort a license. The court agreed and tossed out Petitioner's case. EX2002 (Memorandum Opinion) at 1 (dismissing Neurocrine's declaratory judgment complaint as a failed attempt at a "manufactured spat"). Judge Wolson explained that, "if this is a war, ***only Neurocrine is waging it***." *Id.* at 7. Indeed, the court concluded, "the most [Neurocrine] has pled is that Spruce refused to concede when Neurocrine asked it to do so." *Id.* at 10.

Petitioner now asks to misappropriate Office resources as its next financial harassment venue. No wonder Petitioner failed to identify its failed district court challenge, instead falsely representing that there was no relevant district-court litigation. Pet., 5. Discretionary denial is warranted for Petitioner's abuse of AIA reviews as a tool to harass Spruce. *Magnolia*, IPR2026-00097, Paper 17.

B. Petitioner's Wasteful Harassment is Already Widespread.

Petitioner's use of AIA proceedings as a tool of harassment is further evidenced by its escalating record of attacks. In December of 2024, Petitioner filed a notice of opposition at the European Patent Office against Spruce's European patent EP 3784233. EX2012; *see also* EX2001, 4; EX2003. The following month, Petitioner filed a patent revocation claim against Spruce's UK patent. EX2007. Petitioner also filed the above-discussed district court litigation (Section II.A) as well as a third prior petition for post grant review (PGR2025-00032). These cases are all part of Petitioner's war of "legal and administrative proceedings" to exploit Spruce's "cash burn rate." The Director should deny institution.

III. THE CHALLENGED CLAIMS CURED ANY PERCEIVED DEFECTS FROM NEUROCRINE'S PRIOR PGR CHALLENGES

Neurocrine invokes two prior PGRs against Spruce patents as allegedly establishing that the instant claims are unpatentable (Pet., 4, 8), but those prior PGRs counsel in favor of discretionary denial here. First, the present claims are materially different compared to the claims of those patents challenged in the

previous PGRs. In fact, the present claims specifically address and precisely cure the perceived defects of the prior patents. Second, none of this was lost to the Examiner during prosecution, as the Examiner fully considered the subject matter of the prior PGRs before allowing the present claims. As such, Petitioner's present challenge is both baseless and a poor use of Office resources.

A. The Challenged Claims Cure the Perceived Defect of the Prior PGR Decisions.

In the two prior PGRs that Neurocrine invokes, the Board determined that the claims then at issue were directed to a broad genus of CRF_1 receptor antagonists—including, *inter alia*, peptides, which were never described in the specification. But that reasoning does not apply to the present claims because Spruce conformed to the Board's decision and advanced materially different claims specifically limited to a small handful of small-molecule inhibitors explicitly described in the patent specification.

1. The Present Claims Are Materially Different.

The ultimate basis for invalidating the prior claims in PGR2021-00088 and PGR2022-00025 was that the claims were not limited to small molecule inhibitors, but broadly included peptide-based therapeutics, for which the specification provided no description. *See, e.g.*, PGR2021-00088 Paper 64, 56-57 ("the challenged claims recite only 'a CRF_1 receptor antagonist or a pharmaceutically acceptable salt thereof,' the scope of which also encompasses the much larger

(and, according to Williams) much more effective large-molecule (peptide) CRF_1 receptor antagonists…"); PGR2022-00025 Paper 62, 54-55 (similar).

In contrast, the presently-challenged claims were specifically crafted to cure the very deficiency alleged in the prior PGRs. They are limited to a small handful of small-molecules exemplified in the specification. EX1001, Claims. Because the claims are limited to a small, enumerated set of expressly described compounds rather than some genus, the written-description requirement is satisfied *a fortiori*. As the prior PGR decisions rested on peptide breadth, the prior PGR decisions deserve no persuasive weight for written description of the present claims—which unambiguously exclude the very peptide scope that drove those decisions.

2. The Examiner Fully Considered Petitioner's Challenges Before Issuing the Present Claims.

The Examiner allowed the challenged claims following substantive evaluation of the claimed subject matter. Petitioner's present challenge does nothing more than improperly ask the Office to rehash issues already settled during examination. *See* Section IV.A-B, below (demonstrating that the Examiner thoroughly considered the art and arguments Petitioner now advances).

The presently-challenged claims underwent years of prosecution aimed at addressing the very issue Petitioner now raises. The fact that the present claims were examined specifically in view of the prior PGRs Petitioner now relies upon is

demonstrated by the full file history (EX2009) of the ’490 patent, which Petitioner conspicuously omitted from the petition materials. That full history demonstrates the Examiner was fully aware of Petitioner’s written description challenge during examination. EX2009, 286 (entries 14-18), 548 (same), 1831 (same), 1861, 1845 (same), 1901 (marked as considered by Examiner), 1911 (same), 1938 (entries 27-30), 4173 (same), 4743 (marked as considered by Examiner), 4585 (entry 22), 4598 (same), 4729 (marked as considered by Examiner), 4758 (entry 16), 4770 (same), 4839 (marked as considered by Examiner). Thus, the arguments Petitioner relies upon now from the prior PGRs were considered by the Examiner throughout prosecution of the currently challenged claims. The Office has already determined, in issuing the ’490 patent, that the challenged claims are patentable over the arguments Petitioner presented. Because Spruce successfully cured any perceived deficiency identified in Petitioner’s previous PGRs, Petitioner’s repetitive challenges should be rejected.

B. Allowance of New Claims Under Scrutiny Arising from Petitioner’s Prior PGRs Gave Rise to Strong Settled Expectations.

Rather than undermine the patentability of the present patents, the PGR history actually illustrates strong settled expectations that both Patent Owner and the Office already dealt with the raised issues after a particularly rigorous process over a period of years. As the Office has made clear, it is not merely the issue date

that matters for settled expectations, as they may arise even for recently-issued patents. *Amgen Inc. v. Bristol-Myers Squibb Co.*, IPR2025-00601, -00602, -00603, Paper 9 (July 24, 2025) (informative) ("there may be good reasons why a patent owner has strong settled expectations in a patent that has only been in force for" a short period of time). Here, the presently-challenged claims were allowed following consideration of a series of protracted and highly unusual proceedings that challenged related patents over Petitioner's Section 112 arguments. This issue was front-and-center for the Office for nearly 5 years—culminating in successful prosecution of the instant claims. This nearly five year process for obtaining the instant claims under the direct scrutiny of Petitioner's Section 112 challenges—detailed below—thus gave rise to strong settled expectations in the Office's determination.

Initially, four administrative patent judges serially denied institution in PGR2021-00088 and PGR2022-00025 because Petitioner's own evidence defeated its written description or enablement attacks. PGR2021-00088, Paper 11; PGR2022-00025, Paper 10. Petitioner's own expert witness admitted that a POSA "would, at the time of filing, have been in possession of ***a discrete class of approximately 100 CRF_1 receptor antagonists*** that had already 'been characterized or were in clinical development prior to the filing of the '908 patent.'" PGR2021-00088, Paper 11, 27-28. The Board rightfully credited the self-

defeating admissions against Petitioner's challenges. PGR2022-00025, Paper 10, 33-34; *accord Interactive Commc'ns Int'l, Inc. v. Blackhawk Network Inc.*, IPR2024-00465 Paper 40 (Oct. 9, 2025) (Director vacating FWD and terminating the proceeding where expert admissions called contrary result into question).

Petitioner requested rehearing, and over a period of approximately 26 months the Office never took action. Consolidated Trial Practice Guide, 90 (Nov. 2019) ("The opposing party should not file a response to a request for rehearing absent a request from the Board. The Board envisions that, absent a need for additional briefing by an opponent, requests for rehearing ***will be decided approximately one month after receipt*** of the request."). Then, without notice, former-Director Vidal *sua sponte* granted Director Review and vacated the Board's two previous determinations. Though acknowledging that Petitioner's own declarant and the prior art described CRF_1 receptor antagonists as a well-known and discrete class, former-Director Vidal reversed the non-institution decisions additionally asking if members of that known class had common identified structure. PGR2021-00088 Paper 16; PGR2022-00025 Paper 15. Former-Director Vidal next changed the composition of the panel in the first challenge. PGR2021-00088, Paper 22.

Petitioner then set about rewriting its original challenges mid-trial. First, Petitioner withdrew its original expert who had admitted the genus was a known,

discrete class and replaced him with a substitute expert. Nonetheless, Spruce identified scientific publications (including Petitioner's own publication) with analysis of structural features and identification of structural characteristics common to the known genus—directly addressing former-Director Vidal's concerns. *Accord Teva Pharms. Int'l GmbH v. Eli Lilly & Co.*, 172 F.4th 1367, 1374-77 (Fed. Cir. 2026) (holding Section 112 support existed for claims to use of a genus of compounds when state of art demonstrated the genus was known, absent evidence of unpredictability across the class).

Rather than hold Petitioner to the case presented in its petitions as required (*SAS Inst., Inc. v. Iancu*, 584 U.S. 357 (2018)), the Board in its final written decisions expanded its understanding of the claim scope even further to include, *inter alia*, large-molecule (e.g., peptide) CRF_1 receptor antagonists and found a lack of written description for the same. PGR2021-00088 Paper 64, 55-57; PGR2022-00025 Paper 62, 54-55. This understanding of the claims was never argued during trial. PGR2022-00025, Paper 64, 12 ("[T]he 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***.") (emphasis original).

Faced with such scrutiny and unanticipated construction of its claims in the prior PGRs, Spruce pragmatically turned to curing any perceived deficiency by means of prosecution. *See* Section III.A.1, *supra*. Spruce thus invested years of

effort and significant resources working with the Office to obtain issuance of the presently-challenged claims, all after resolution of the prior PGRs. As explained above (*see* Section III.A.2, *supra*), the Examiner issued the claims fully aware of the prior PGR trial records. The fact that the Examiner allowed these claims despite the rigid scrutiny arising from the prior PGRs demonstrates there are unusually strong settled expectations in these patents. Relying on that rigorous process, Spruce has continued to invest resources in CAH therapeutics. Petitioner identifies no adequate justification for unsettling the expectations generated through nearly ***five years*** of work together with the Office.

IV. PETITIONER'S PRESENT CHALLENGE SHOULD BE REJECTED UNDER 35 U.S.C. §325(D) AS CUMULATIVE AND WASTEFUL.

Petitioner has asked the Board to use its limited resources to revisit issues already resolved by the Office. But Office resources should be used only in instances where there is a "substantial showing of apparent examiner error." *Magnolia*, IPR2026-00097 Paper 17, 6. The "central purpose of" AIA reviews "is to determine whether the patent at issue may have been improvidently granted," and this is why Congress provided the Office with institution discretion. *Id.* Here, Petitioner merely seeks to rehash issues already resolved by the Office during informed examination and fails to demonstrate apparent examiner error.

A. The Office Already Considered Section 112 During Prosecution

Despite Petitioner's failure to submit the full prosecution history here, the more fulsome record (EX2009) amply demonstrates that the Office already considered the same Section 112 issues Petitioner asks to re-hash here. Petitioner reliance on the final written decisions from PGR2021-00088 and PGR2022-00025 is misplaced. *See, e.g.*, Pet., 14 ("like the claims found unpatentable in the previous PGRs, the claims in these newly issued patents encompass CRF_1 receptor antagonists that the named inventors failed to describe and enable"). The claims here are materially different. Moreover, these final written decisions were explicitly considered by the Office during prosecution of the instant patents. EX2009, 286 (entries 14-18), 548 (same), 1831 (same), 1861, 1845 (same), 1901 (marked as considered by Examiner), 1911 (same), 1938 (entries 27-30), 4173 (same), 4743 (marked as considered by Examiner). The Examiner also independently evaluated written description for the new claims. For example, the Examiner evaluated whether provisional applications supported treating of menstrual irregularities during prosecution of the challenged patent. *See, e.g.*, EX2009, 1864. The Office thus already evaluated Section 112 support for the challenged claims.

B. No Demonstration of Material Error

Petitioner has failed to demonstrate material error in issuance of the '490 patent. Conversely, "if the alleged error is a disagreement with a specific finding of record by the Office, then ordinarily the petitioner's required showing of material error must overcome persuasively that specific finding of record." *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469 Paper 6, at 10-11 (Feb. 13, 2020) (precedential). Instead, there is "a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown." *Id.* at 9. Here, Petitioner provides nothing but disagreement with the Office's previous determinations.

Petitioner begins with conclusory allegations that the Examiner erred by allowing the claims. *See*, Pet., 4 ("The '490 patent should not have issued, and the Examiner erred in allowing its overly broad claims."). But such conclusory pronouncement fails to satisfy Petitioner's burden to demonstrate error in the Examiner's position. *Ex parte Belinne*, 2009-004693 (PTAB, Aug. 10, 2009) (informative). Conclusory assertions are insufficient to demonstrate material error by the Office. *TankLogix, LLC v. SitePro, Inc.*, IPR2025-00761, Paper 10 at 2-3 (Sept. 3, 2025) (citing *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 5 (May 19, 2025) (precedential)).

Second, Petitioner alleges the "Examiner erred in allowing the amendments to the specification and claims" because the Examiner approved the correction of a minor typographical error depicting an impossible quadruple bond where a triple bond was instead intended. Pet., 45. Again, Petitioner's incomplete prosecution history submission obscures the truth. As explained during examination, the amendment was consistent with a Certificate of Correction previously accepted by the Office for related U.S. Pat. No. 11,304,950. EX2009, 4322, 4702. In a copending application, the Examiner observed the corrections were "to correct typographical errors" (EX2008, 4551), and the Examiner expressly considered and evaluated the amendments to the '490 specification, observing they were "acknowledged and accepted." EX2009, 4702. There is no genuine question that the chemical structure (with the triple bond) is the correct structure. EX2011. Once again, Petitioner does not demonstrate error, only desire to harass.

V. CONCLUSION

AIA reviews are not a tool for harassment and the PTAB is not a forum for rehashing prior Office decisions. To determine otherwise would invite a waste of Office resources. Patent Owner respectfully requests that the Director exercise discretion to deny institution of the petition.

Respectfully submitted,

Date: August 18, 2026

/ Michael T. Rosato /
Michael T. Rosato, Lead Counsel
Reg. No. 52,182

VI. APPENDIX

Exhibit No.	Description
2001	*Neurocrine Biosciences, Inc. v. Spruce Biosciences, Inc.*, No. 1:25-cv-00059 (D. Del. June 9, 2025), ECF No. 19 (Motion to Dismiss).
2002	*Neurocrine Biosciences, Inc. v. Spruce Biosciences, Inc.*, No. 1:25-cv-00059 (D. Del. June 9, 2025), ECF No. 26 (Memorandum Opinion).
2003	E-mail Letter from Mike Morin, Counsel representing Neurocrine Biosciences, to Dr. Javier Szwarcberg, CEO Spruce Biosciences Inc. (Dec. 10, 2024).
2004	E-mail from Mike Morin, Counsel representing Neurocrine Biosciences, to Michael Rosato, Counsel representing Spruce Biosciences Inc. (Jan. 11, 2025).
2005	E-mail Letter from Mike Morin, Counsel representing Neurocrine Biosciences, to Michael Rosato, Counsel representing Spruce Biosciences Inc. (Jan. 6, 2025).
2006	*Neurocrine Biosciences, Inc. v. Spruce Biosciences, Inc.*, No. 1:25-cv-00059 (D. Del. June 9, 2025), ECF No. 1 (Complaint).
2007	*Neurocrine Biosciences, Inc. v. Spruce Biosciences, Inc.*, CASEBOARD (Jan. 30, 2025), https://caseboard.io/cases/ac09fc0e-6e6e-497b-adc5-4bc46d1541be.
2008	File History – US Pat. No. 12,569,491.
2009	File History – US Pat. No. 12,569,490.
2010	File History – US Pat. No. 12,576,084.
2011	Danielle Gully et al., *4-(2-Chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]5-methyl-N-(2-propynyl)-1,3-thiazol-2-amine Hydrochloride*

	(SSR125543A): A Potent and Selective Corticotrophin-Releasing Factor1 Receptor Antagonist. I. Biochemical and Pharmacological Characterization, 301(1) J. PHARMACOLOGY & EXPERIMENTAL THERAPEUTICS 322-332 (2002).
2012	Notice of Opposition Proceedings to EPO Pat. No. 3784233

CERTIFICATE OF SERVICE

The undersigned certifies that the foregoing Patent Owner's Brief In Support of Discretionary Denial and accompanying Exhibits 2001-2012 were served on August 18, 2026, on the Petitioner at the electronic correspondence address of the Petitioner as follows:

Kristi L. R. Sawert
Robert M. Oakes
W. Karl Renner
Katie E. Hyma
FISH & RICHARDSON P.C.
PGR47291-0012PS1@fr.com

Dated: August 18, 2026

/ Michael T. Rosato /
Michael T. Rosato, Lead Counsel
Reg. No. 52,182