

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ASCENDIS PHARMA A/S,
Petitioner,

v.

BIOMARIN PHARMACEUTICAL INC.,
Patent Owner.

Case PGR2026-00013
Patent No. 12,233,106 B2

PATENT OWNER'S BRIEF REQUESTING DISCRETIONARY DENIAL

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Exhibit No.	Description	Previously Submitted
2001	USITC Inv. No. 337-TA-1447, Order No. 25: Amending Procedural Schedule (December 16, 2025), EDIS Doc. ID. 866614	
2002	USITC Investigations Database System, Status of Investigation 337-1447, https://ids.usitc.gov/case/8276/investigation/8728 (last accessed January 20, 2026)	
2003	RESERVED	
2004	U.S. Reissue Patent No. 48,267	
2005	USITC Inv. No. 337-TA-1447, Amended Complaint (August 22, 2025), EDIS Doc. ID. 860269	
2006	USITC Inv. No. 337-TA-1447, Disputed and Agreed Claim Constructions (September 23, 2025), EDIS Doc. ID 862675	
2007	RESERVED	
2008	RESERVED	
2009	RESERVED	
2010	RESERVED	
2011	USITC Inv. No. 337-TA-1447, Order No. 15: Initial Determination Granting Complainant's (1) Motion to Declassify and (2) Motion to Amend the Complaint and Notice of Investigation (August 14, 2025), EDIS Doc. ID. 861044	
2012	FDA Guidance for Industry, General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products (July 2022) at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-clinical-pharmacology-considerations-neonatal-studies-drugs-and-biological-products-guidance , and https://www.fda.gov/media/129532/download (last accessed January 27, 2026)	
2013	Sian Gaze, Best Practice for Medicines Use in Neonates, Pharmaceutical Journal (May 7, 2024) at https://pharmaceutical-journal.com/article/ld/best-	

	practice-for-medicines-use-in-neonates (last accessed January 27, 2026)	
2014	March 31, 2025 Ascendis Press Release at https://investors.ascendispharma.com/news-releases/news-release-details/ascendis-submits-us-nda-transcon-cnp-navepegritide-treatment (last accessed January 27, 2026)	
2015	November 25, 2025 Ascendis Press Release at https://investors.ascendispharma.com/news-releases/news-release-details/ascendis-announces-extension-fda-review-period-transcon-cnp (last accessed January 27, 2026)	
2016	Clinical Trial NCT06079398 (ASND0030) at https://clinicaltrials.gov/study/NCT06079398 (last accessed January 27, 2026)	
2017	Savarirayan (2024), <i>Vosoritide therapy in children with achondroplasia aged 3-59 months: a multinational, randomised, double-blind, placebo-controlled, phase 2 trial</i> , Lancet Child Adolesc. Health, 8(1):40-50	
2018	USITC Inv. No. 337-TA-1447, Commission Investigative Staff's Claim Construction Brief (December 1, 2025), EDIS Doc. ID. 866257	

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<i>Becton, Dickinson & Co. v. B. Braun Melsungen AG,</i> IPR2017-01586, Paper 8 (PTAB Dec. 15, 2017)	10
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<i>Tesla, Inc. v. Intellectual Ventures II LLC</i> , IPR2025-00340, Paper 18 (Director Nov. 5, 2025).....	2, 3, 4
<i>Worlds Inc. v. Bungie, Inc.</i> , 903 F.3d 1237 (Fed. Cir. 2018)	7
<i>Yangtze Memory Technologies Company, Ltd. v. Micron Technology, Inc.</i> , IPR2025-00098, Paper 38 (Director Jan. 15, 2026)	7
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<i>Certain Drug Products Containing C-Type Natriuretic Peptide Variants</i> , 90 Fed. Reg. 44843, 44843–44 (Sept. 17, 2025)	8
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I. INTRODUCTION

Patent Owner BioMarin Pharmaceutical Inc. (“BioMarin”) respectfully requests that the Director deny institution of Petitioner Ascendis Pharma A/S (“Ascendis”)’s Petition challenging U.S. Patent No. 12,233,106 (the “’106 patent,” Ex. 1001). Discretionary denial is warranted due to claim construction inconsistency, unnamed real parties-in-interest (RPIs), and 35 U.S.C. § 325(d).

First, Ascendis has taken materially different positions in this PGR compared to the co-pending U.S. International Trade Commission (“ITC”) investigation No. 337-TA-1447 (“ITC investigation”), which involves BioMarin’s Reissue Patent No. 48,267 (“RE48,267,” Ex. 2004). In the ITC, Respondent Ascendis has construed the claim term “CNP variant” to require a functional peptide—one “capable of binding to and activating NPR-B, and thereby inducing cGMP production.” (Ex. 2006, Appendix A.) BioMarin’s “ordinary and customary meaning”—a variant of C-type natriuretic peptide (CNP)—was insufficient for Ascendis, who construed the term to require the presence of specific peptides and functionality. (*See* Ex. 2018, 18.) But apparently Ascendis did not feel the same need in this PGR even though the term “CNP variant” is recited in challenged independent claim 1. (Ex. 1001, 63:39-40 (“composition comprising a C-type natriuretic peptide (CNP) variant”).) Instead, Ascendis appears to have applied the plain and ordinary meaning for that term. (*See* Petition, 23-25; Ex. 1003, ¶¶52-56.)

The PGR thus effectively asks the Board to apply an ordinary-meaning approach that omits the functional limitation Ascendis insists upon in the ITC—inviting conflicting determinations.

As explained below in Section II, Ascendis’ strategic choice in not construing CNP variant in this PGR appears to have been motivated by the lack of relevant disclosure in the prior art on the critical issue of reasonable expectation of success. But Ascendis’ unexplained, forum-dependent shifts undermine predictability and uniformity in post-grant proceedings warranting denial of the instant Petition. *See Revvo Techs., Inc. v. Cerebrum Sensor Techs., Inc.*, IPR2025-00632, Paper 20 (Director Nov. 3, 2025) (precedential); *Tesla, Inc. v. Intellectual Ventures II LLC*, IPR2025-00340, Paper 18 (Director Nov. 5, 2025) (informative). Such a result is especially warranted here because the ITC investigation is expected to reach a Final Determination well before the Board’s Final Written Decision.¹

Second, the Petition fails to identify all real parties in interest. Entities with direct and concrete commercial interests in the outcome of this proceeding—

¹ The ITC investigation is actively proceeding, with a claim construction hearing scheduled for February 6, 2026, an evidentiary hearing scheduled for April 20–24, 2026, an Initial Determination targeted for August 21, 2026, and a Final Determination targeted for December 21, 2026. (Ex. 2001; Ex. 2002.)

arising from manufacturing and supply relationships tied to the accused products in the parallel ITC investigation—were known to Ascendis at the time of filing yet were not disclosed. That failure independently warrants denial.

Third, discretionary denial is independently warranted under 35 U.S.C. § 325(d). The Petition relies on the same core prior art and substantially the same arguments that were presented to and considered by the Examiner during prosecution, including Bullens (Ex. 1008), Wendt-242 (Ex. 1023), and Savarirayan (Ex. 1005). Ascendis does not identify any material examiner error; the Petition merely reweighs the same evidence and urges a different conclusion—precisely the type of hindsight-driven prosecution do-over that § 325(d) is designed to prevent. The Petition should also be denied because the challenged '106 patent is now being litigated in parallel in district court.

II. THE PETITION SHOULD BE DENIED TO AVOID FORUM-DEPENDENT POSITIONS

The Director has prohibited Petitioners from taking unexplained, forum-dependent shifts without explanation. *See Revvo*, IPR2025-00632, Paper 20; *Tesla, Inc.*, IPR2025-00340, Paper 18. These decisions are designed to minimize inconsistency between forums and to discourage Petitioners from seeking broader constructions at the Board to support invalidity while seeking narrower constructions in litigation to avoid infringement. These concerns are squarely

implicated here.

RE48,267, just like the '106 patent, relates to C-type natriuretic peptide (“CNP”) variants and methods of using CNP variants to treat bone-related disorders, such as skeletal dysplasias (e.g., achondroplasia). (Ex. 2004 and Ex. 1001, 1, Field of the Disclosure.) In the ITC investigation, BioMarin has asserted, *inter alia*, RE48,267 claim 15 (Ex. 2005, 1), which recites macromolecules capable of releasing specific CNP variants, including Pro-Gly-CNP37; CNP-40 through CNP-30; CNP37 (M32N); Pro-, Met-, Gly-, Met-Gly-CNP37; Gly-CNP37 (M32N); HSA-CNP27; CNP27 (K4,5,9R); and PEG1K-, PEO12-, PEO24-conjugated CNP27 (K4, 5, 9R) variants. (Ex. 2004, 269:64-270:65.) Claim 1 of the '106 Patent recites the *same* CNP variants while expressly claiming their use in the treatment of infants “about 0 month to about 2 years old.” (*Compare* Ex. 1001, claim 1, *with* Ex. 2004, claim 15.) While Ascendis construes “CNP variant” in the ITC investigation, Ascendis does not construe the term in this PGR nor explain why a POSA would have an expectation of success under Ascendis’ construction. Under *Revvo* and *Tesla*, such an inconsistency warrants denial of the Petition.

In the ITC investigation, Ascendis advances a construction of the term “CNP variant” that imposes a functional requirement—“capable of binding to and activating NPR-B, and thereby inducing cGMP production.” (Ex. 2006, Appendix A.) Ascendis disagrees with BioMarin’s proposed plain and ordinary meaning

construction in the ITC investigation. (*Id.*) Unlike the ITC, Ascendis affirmatively proceeds under an “ordinary and customary meaning” approach and does not apply that same functional requirement to “CNP variant” in the PGR. (Petition, 23–25.)

Ascendis does not explain why its functional interpretation of “CNP variant” is not warranted in the instant PGR petition and why the Board should instead apply the plain and ordinary meaning for this term. Ascendis does not explain why it did not offer a construction for CNP variant tied to cGMP production in this PGR despite disclosures in the ’106 patent discussing CNP variants and cGMP stimulation. (*See, e.g.*, Ex. 1001, 2:31-34 (“CNP binds to and activates natriuretic peptide receptor B (NPR-B) . . . resulting in higher . . . (cGMP) levels”), 2:31-34; *see also id.*, 11:41-48, 12:37-44.) Nor does Ascendis explain why the claim construction principles that led Ascendis to construe the term in the ITC should not also apply in this PGR.

Conveniently, Ascendis treats the claim requirements as satisfied in this PGR without requiring proof, as part of claim scope, that a claimed variant binds to and activates NPR-B or induces cGMP production in the claimed infant population. For obviousness, Ascendis draws from references to ongoing or anticipated pediatric studies, notwithstanding that the efficacy data in those references concerns children older than the claimed infant population (“about 0 month to about 2 years old”). (Petition, 17–19, 27–29, 48–50.) Ascendis argues that Höglér

and Savarirayan teach or suggest a method of treating achondroplasia in infants because they describe results of clinical studies treating children older than 5 years old with *vosoritide (also known as Pro-Gly-CNP)* and Högler proposes starting treatment “shortly after, or before, birth” (Ex. 1007, 106), while Savarirayan mentions that a clinical study of administering vosoritide in infants and younger children with achondroplasia has been initiated. (Ex. 1005, 34; Petition, 25-29.) Ascendis also argues that Pauli and Savarirayan teach or suggest a method of treating achondroplasia in infants, because Pauli mentions that there are complications associated with achondroplasia in infants and a clinical study of administering vosoritide in infants and younger children with achondroplasia has been initiated. (Petition, 46-50.)

However, Ascendis fails to adequately explain that any of Högler, Pauli, and Savarirayan teaches or suggests treatments with CNP variants that were “capable of binding to and activating NPR-B, and thereby inducing cGMP production” in an “amount effective” to treat skeletal dysplasia *in an infant aged 0 month to about 2 years old*, as claimed. Indeed, there is no data in Pauli, Högler and Savarirayan, suggesting that vosoritide (also known as Pro-Gly-CNP), the drug relied upon in the Petition for the claimed “CNP variant,” would have been expected to activate NPR-B, and induce cGMP production *in an infant aged 0 month to about 2 years old* sufficient to treat skeletal dysplasia. This is important because infants differ

materially from older children in pharmacokinetics and pharmacodynamics, including drug absorption, distribution, metabolism, and elimination. (Ex. 2012, 6-11; Ex. 2013.)

By asking the Board to evaluate the asserted prior art under a construction that omits a functional limitation Ascendis insists is mandatory in the ITC, Ascendis advances materially different claim scope across forums—inviting conflicting determinations and warranting discretionary denial. Also, the ITC is projected to reach a final Commission determination before the Board would issue a Final Written Decision in this PGR. Discretionary denial is warranted to avoid placing the Board on a foreseeable collision course with the ITC.

III. THE PETITION SHOULD BE DENIED FOR FAILING TO IDENTIFY ALL REAL PARTIES IN INTEREST

A petition that fails to identify all real parties in interest (“RPIs”) is not in condition for consideration. *Corning Optical Communications RF, LLC v. PPC Broadband, Inc.*, IPR2014-00440, Paper 68 (PTAB Aug. 18, 2015) (precedential). Once a patent owner produces some evidence that an unnamed entity may be an RPI, Petitioner bears the burden to provide sufficient clarity to permit the Board to determine whether the statutory requirement is met. *Worlds Inc. v. Bungie, Inc.*, 903 F.3d 1237, 1242–44 (Fed. Cir. 2018); *Yangtze Memory Technologies Company, Ltd. v. Micron Technology, Inc.*, IPR2025-00098, Paper 38 (Director

Jan. 15, 2026) (informative). The record establishes that Bachem AG (“Bachem”) and Wacker Biotech GmbH (“Wacker”) have direct, concrete interests in the outcome of this proceeding but have not been named as RPIs.

BioMarin’s patent RE48,267 is being asserted in the ITC investigation concerning drug products containing C-type natriuretic peptide variant, “commercially known as ‘TransCon CNP.’” (Ex. 2005, ¶¶41-42.). Asserted claim 15 of RE48,267 overlaps in subject matter with the challenged claims of the ’106 patent, as explained above in Section II. In the ITC investigation, Wacker was named as a respondent at institution, and Bachem was later added as a respondent when the Commission amended the notice of investigation. *Certain Drug Products Containing C-Type Natriuretic Peptide Variants*, 90 Fed. Reg. 19532–33 (May 8, 2025); *id.*, 90 Fed. Reg. 44843, 44843–44 (Sept. 17, 2025).

Ascendis’s own commercial arrangements further confirm that *at least* Bachem and Wacker have a direct commercial interest in the relief sought in this proceeding. As explained in the ITC Amended Complaint filed on August 22, 2025, “Wacker is the sole manufacturer and supplier of TransCon CNP drug substance to” Ascendis. (Ex. 2005, ¶24.) Bachem is a “supplier” with a “role in the supply chain for the accused product[,]” *i.e.*, “TransCon CNP.” (Ex. 2011, 1, 3.) But Ascendis did not acknowledge its relationship with Wacker and Bachem in the Petition, let alone explain why they are not RPIs. (*See* Petition, 89.)

Ascendis submitted to the U.S. Food and Drug Administration (“FDA”) a New Drug Application for TransCon CNP on March 31, 2025 (Ex. 2014), and the FDA’s review is approaching a near-term decision date, including a PDUFA goal-date extension to February 28, 2026 (Ex. 2015). Ascendis also is recruiting for *an infant (0 to <2 years)* clinical trial for TransCon CNP. (Ex. 2016.) Those facts underscore that challenging the ’106 patent would directly benefit Wacker and Bachem by reducing BioMarin’s U.S. patent protection constraining the same accused product and supply chain.

Taken together, this record places the identification of real parties in interest into dispute and to trigger Ascendis’s burden to provide clarity on RPI. Ascendis filed the Petition on November 24, 2025—after Wacker had been named as a respondent at institution on May 8, 2025, and Bachem had been added as a respondent when the Commission amended the notice of investigation. Thus, at the time of filing, Ascendis had notice of Wacker and Bachem’s role, but provided no explanation regarding their status in the Petition. This failure warrants denial of the Petition.

IV. THE PETITION SHOULD BE DENIED UNDER 35 U.S.C. § 325(d)

Discretionary denial pursuant to § 325(d) is warranted under the two-part framework articulated in *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (PTAB Feb. 13, 2020) (precedential); *see*

also Becton, Dickinson & Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential).

A. Prong 1 – The Asserted Prior Art and Arguments Were Previously Presented

1. Bullens (Ex. 1008), Wendt-242 (Ex. 1023), and Savarirayan (Ex. 1005) Were Before the Examiner

Ascendis admits Bullens was applied by the Examiner during prosecution. (Petition, 21.) Ascendis admits Wendt-242 was submitted in an Information Disclosure Statement (“IDS”). (*Id.*, 8.) Wendt-242 is also cumulative of Wendt-639 (Ex. 1046), which the Examiner expressly applied during prosecution. (*Infra*, Section IV.B.2.) Specifically, the Examiner rejected the pending claims as obvious over Bullens in view of Wendt-639. (Ex. 1002, 906–911.) The Examiner asserted that Bullens disclosed “treating patients with skeletal dysplasia,” that Wendt-639 disclosed “CNP variants ... can be administered ... to treat ... achondroplasia,” and that “the ideal age range of achondroplasia patients will be from infant (<1 year of age) to pre-adolescent (<13 years of age).” (*Id.*, 907–910.)

BioMarin amended the claims and argued that the cited art did not provide a reasonable expectation of success for treating the claimed subpopulation of subjects from about 0 month to about 2 years old, and that the specification disclosed unexpected benefits. (*Id.*, 935–937.) The Examiner agreed, expressly concluding in the Notice of Allowance that “one of ordinary skill in the art would

not have predicted the results in children from about 0 month old to about 2 years old of instant application.” (*Id.*, 966.) Ascendis now seeks to relitigate that same issue using the same core disclosures.

Ascendis admits Savarirayan was submitted in an IDS during prosecution. (Petition, 8.) Moreover, the Examiner acknowledged a Savarirayan publication from 2024 in the Notice of Allowance. (Ex. 1002, 936, 966.) That publication cites the same Savarirayan paper from 2019 (*i.e.*, Ex. 1005) relied upon by Ascendis here, confirming that the IDS submission placed the substance of the relied-upon disclosure before the Office. (Ex. 2017, 41, 50 n. 4.)

**2. Pauli (Ex. 1006) and Högler (Ex. 1007)
Are cumulative of Art Previously Considered**

Pauli is cumulative of prior art previously considered by the Office. Ascendis acknowledges that Savarirayan disclosed an ongoing vosoritide trial in infants and younger children and that “Pauli similarly disclosed” vosoritide in an expanded Phase 2 trial involving infants and young children. (Petition, 18-19.) Ascendis further concedes that “Savarirayan discloses the results of the same clinical studies referenced in Pauli.” (*Id.*, 49.) Pauli therefore presents no materially different or more pertinent technical disclosure than Savarirayan, which was before the Examiner. Like Savarirayan, Pauli discusses the clinical motivation for early-life intervention without reporting completed clinical trials demonstrating

safety or efficacy of C-type natriuretic peptide variants in the claimed 0–2 year-old population. (Ex. 1006, 9–10.) Pauli thus adds no data resolving the unpredictability associated with infant treatment that the Examiner expressly identified and relied upon in allowing the claims. (Ex. 1002, 966.) Pauli is thus cumulative of Savarirayan and adds no completed infant efficacy data bearing on reasonable expectation of success.

Ascendis likewise acknowledges that “Savarirayan reports the results of the same clinical studies disclosed in Högler.” (Petition, 28.) Högler is a review article that restates the same primary data already before the Office and expressly cites Savarirayan. (Ex. 1007, 110 n.38.) Högler is also cumulative of Wendt-639, which the Examiner applied during prosecution. The Examiner asserted that Wendt-639 teaches that infants fall within an “ideal” age range for treatment of achondroplasia using C-type natriuretic peptide variants (Ex. 1002, 909), while Högler similarly discusses that because complications from foramen magnum stenosis occur “very early in life, the timing of future interventions would need to be shortly after, or before, birth,” yet the only efficacy data he reports are from the same underlying studies disclosed in Savarirayan (Ex. 1007, 106, 108, 110 n.38). Neither reference resolves the unpredictability associated with treating the claimed 0–2 year-old population, which the Examiner credited during prosecution. (Ex. 1002, 966.) Högler is therefore cumulative of Savarirayan and Wendt-639 and

likewise adds no completed infant efficacy data bearing on reasonable expectation of success.

3. The Examiner Considered § 112 Issues

The Examiner previously considered compliance with 35 U.S.C. § 112 during prosecution. (Ex. 1002, 904–906.) Indeed, the Examiner is presumed to have considered “each claim . . . for compliance with every statutory requirement for patentability,” including those under § 112. M.P.E.P. § 2103 (I).

B. Prong 2 – Ascendis Does Not Show Material Error

Because Ascendis relies on the same or substantially the same prior art and arguments previously considered during prosecution, it bears the burden under *Advanced Bionics* of demonstrating that the Office erred in a manner material to patentability. Ascendis cannot meet that burden.

1. The Examiner’s Express Finding of Unpredictability in Treating the Claimed Infant Population Was Reasonable (Grounds 1–4)

The Examiner expressly addressed—and resolved—the precise issue Ascendis now seeks to relitigate: whether a person of ordinary skill in the art would have reasonably expected success in treating the claimed 0–2 year-old population. In the Notice of Allowance, the Examiner concluded that “one of ordinary skill in the art would not have predicted the results in children from about 0 month old to about 2 years old.” (Ex. 1002, 966.) That express finding confirms that the

Examiner evaluated the asserted prior art, considered the clinical context, and determined that success in the claimed infant subpopulation was unpredictable.

Ascendis identifies no misapprehension of the prior art, no overlooked disclosure, and no misapplication of law. Instead, it merely reweighs the same evidence and urges a different conclusion regarding reasonable expectation of success—precisely the type of hindsight-driven reassessment that § 325(d) is intended to prevent. Where, as here, the Examiner considered the art and arguments during examination, a petitioner must show that no reasonable examiner could have concluded that the claims were patentable. If reasonable minds could disagree regarding the treatment of the art or the associated arguments, the Office has not erred in a manner material to patentability. *Ecto World, LLC and SV3, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 (PTAB May 19, 2025) (precedential). The Board has exercised discretion under § 325(d) where a petitioner merely repackages arguments already considered during prosecution. *PRISM Pharma Co., Ltd. v. Choongwae Pharma Corp.*, IPR2014-00315, Paper 14 (PTAB July 8, 2014) (informative). Discretionary denial is likewise appropriate where, as here, the petition amounts to a prosecution do-over based on the same prior art combinations previously evaluated by the Examiner. *Cultec, Inc. v. StormTech LLC*, IPR2017-00777, Paper 7 (PTAB Aug. 22, 2017) (informative).

The Examiner's unpredictability finding was reasonable. Treatment of very young infants raised materially different clinical and safety considerations than treatment of older pediatric patients. Pauli discloses that "some infants with achondroplasia will die because of craniocervical junction issues" and "that craniocervical compression can cause non-lethal but severe respiratory problems." (Ex. 1006, 9–10.) Höglér similarly identifies infancy as a uniquely vulnerable period, emphasizing early-arising complications, incomplete understanding of growth-plate biology, and risks such as foramen magnum stenosis, sleep-disordered breathing, and death in the first year of life. (Ex. 1007, 105-106, 109.) Consistent with this uncertainty, Savarirayan reports evaluating "the safety and side-effect profile of vosoritide in children (5 to 14 years of age) with achondroplasia," while describing "ongoing" clinical trials "of vosoritide in infants." (Ex. 1005, 25, 34.) These considerations reinforce deference to the Examiner's contemporaneous judgment in an area of substantial clinical uncertainty. At the time of examination, the record reflected heightened safety concerns in infants and no completed clinical trials demonstrating efficacy in the claimed 0–2 year-old population. Section 325(d) is designed to prevent hindsight-driven reweighing of that kind of examiner determination.

In unpredictable medical contexts, the Board has declined to revisit Examiner determinations under § 325(d) where the Examiner "considered fully"

the relevant issues and the petitioner failed to present new evidence or arguments demonstrating that the determination was unreasonable. *Hospira, Inc. v. Genentech, Inc.*, IPR2017-00739, Paper 16 (PTAB July 27, 2017) (informative). Because Pauli and Högler merely summarize or recharacterize studies and motivations already before the Office—and because Ascendis relies primarily on expert testimony that does not add materially new technical disclosure beyond that previously considered—these references do not meaningfully distinguish the prior art for purposes of § 325(d). *Puma SE v. Nike, Inc.*, IPR2019-01042, Paper 10 at 20 (PTAB Oct. 31, 2019) (informative) (explaining that reliance on a declaration that merely disagrees with the Examiner’s evaluation, without identifying error, does not supply meaningful additional evidence under the § 325(d) analysis).

Grounds 1–4 repackage the same reasonable-expectation-of-success dispute the Examiner resolved in allowing the claims for the 0–2 year-old subpopulation. Reweighing the same evidence and motivations does not establish material error.

2. Ascendis’s Anticipation Theory Relies on Expert Reconstruction Rather Than New Disclosure in Wendt-242 (Ground 5)

Ground 5 does not identify any material error in the Office’s consideration of Wendt-242. The Petition relies on Examples 13 and 19 in Wendt-242 for anticipation. (Petition, 63.) Example 13 relates to mice studies as opposed to studies in infants, as claimed. (See Ex. 1023, 126:20-127:52.) As for Example 19,

it has the same relevant disclosures as Example 12 in Wendt-639. (*Compare* Ex. 1023, 139:4-140:47 (Wendt-242, Example 19), *with* Ex. 1046, 106:12-108:2 (Wendt-639, Example 12).) The Examiner expressly relied upon Example 12 in Wendt-639 during prosecution and did not find it anticipatory. (Ex. 1002, 907–11 (relying on Wendt-639’s disclosure of “infant (<1 year of age) to pre-adolescent (<13 years of age)”)).) The Petition attempts to repackage those same disclosures by overlaying expert age-mapping and efficacy inferences onto Wendt’s juvenile-mouse and prophetic proposals. (Petition, 63-65; Ex. 1003, ¶¶ 163–180.) That reframing is not a showing that the Examiner’s determination was unreasonable, and it does not establish material error under § 325(d). Moreover, the Petition’s anticipation theory depends on expert inference to supply key aspects of the claimed infant-treatment teachings, underscoring that Ground 5 is a prosecution do-over—not a showing of material examination error.

3. Ascendis’s Enablement Challenge Does Not Identify Any Material Examiner Error (Ground 6)

Ascendis’s § 112 challenges do not identify any material error in the Examiner’s enablement determination. Ascendis ignores that enablement must be analyzed in light of the information in the specification, which includes, *inter alia*, a working example. (Ex. 1001, 39:27-50:17.) Ascendis does not identify any misapprehension of the claims, any overlooked disclosure, or any misapplication of

law by the Examiner. At most, the Petition repackages disagreement with the Examiner’s judgment regarding claim scope and enablement as “undue experimentation,” precisely the hindsight-driven reevaluation § 325(d) is designed to prevent. *Kayak Software Corp. v. International Business Machines Corp.*, CBM2016-00075, Paper 16 (PTAB Dec. 15, 2016) (informative) (exercising § 325(d) where the petition relied on additional references and arguments that did not materially change the issues already considered during examination).

Ascendis argues that the claims are broad—citing, for example, “subjects” and many “skeletal dysplasias”—and contends that the specification’s disclosures would require “undue experimentation.” (Petition, 75–87.) But the Petition does not identify any specific claim element that the Examiner misunderstood, any disclosure the Examiner overlooked, or any misapplication of the enablement standard that would amount to material error under § 325(d). Generalized breadth criticisms and assertions about hypothetical experimentation do not supply the missing showing of material examination error required by *Advanced Bionics*.

4. Ascendis’s Improper Dependency Challenge Does Not Identify Any Material Examiner Error (Ground 7)

The Examiner previously considered compliance with 35 U.S.C. § 112 during prosecution, rejecting original dependent claims for improper dependency. (Ex. 1002, 904–905.) Ascendis does not identify any material error in that

determination. Ascendis contends that claim 8 is improper because it recites that dosage “may be decreased.” (Petition, 87–89.) That contention is, at most, a new characterization of claim language already examined and does not establish any misapplication of § 112 or other material examination error. Moreover, claim 8 does not introduce an optional inconsistency; it specifies a dosage-adjustment regimen contingent on the patient reaching age two, narrowing the claim to a particular clinical protocol and remaining fully consistent with Claim 5.

**C. Discretionary Denial Is Warranted to
Avoid Inefficient Adjudication of Redundant Grounds**

Finally, discretionary denial is warranted for reasons of efficiency and finality. The Board must institute on all asserted grounds or none, *SAS Institute Inc. v. Iancu*, 584 U.S. 357, 364–65 (2018), and institution triggers full adjudication of all instituted claims and grounds in a final written decision. Here, it would not be efficient to require the Board and BioMarin to expend substantial resources adjudicating numerous claims and grounds that repackage issues already addressed during prosecution and are subject to discretionary denial. *See Zhuhai CosMX Battery Co., Ltd. v. Ningde Amperex Technology Limited*, IPR2025-00405, Paper 24 (Director Oct. 15, 2025).

V. THE ’106 PATENT IS INVOLVED IN A PARALLEL LITIGATION

BioMarin has now asserted the challenged ’106 patent in district court, where validity will be litigated and adjudicated in parallel. *BioMarin Pharm. Inc.*

v. Zydus Lifesciences Ltd., No. 2:26-cv-01005-RMB (D.N.J. Feb. 2, 2026).

Therefore, institution would be inefficient and would create a meaningful risk of inconsistent outcomes because the district court will potentially address the same invalidity issues on an overlapping schedule after the parties and court have begun investing resources. The Director should therefore deny institution and allow the district court action to proceed as the sole forum for resolving validity.

VI. CONCLUSION

BioMarin respectfully requests that the Director deny the Petition.

Dated: February 3, 2026

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that I caused to be served on the counsel identified below a true and correct copy of the foregoing Patent Owner's Brief Requesting Discretionary Denial of Institution by electronic means on February 3, 2026:

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