

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
U.S. Patent No. 12,233,106

**PETITIONER'S BRIEF OPPOSING
DISCRETIONARY DENIAL**

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PETITIONER'S UPDATED EXHIBIT LIST

Exhibit No.	Description
1001	U.S. Patent No. 12,233,106 to Day et al., issued February 25, 2025
1002	Prosecution History of U.S. Patent No. 12,233,106
1003	Declaration of Dr. Mary Jennifer Abuzzahab, M.D.
1004	<i>Curriculum Vitae</i> of Dr. Mary Jennifer Abuzzahab, M.D.
1005	Savarirayan, Ravi, et al. "C-type natriuretic peptide analogue therapy in children with achondroplasia." <i>New England Journal of Medicine</i> 381: 25-35 (2019).
1006	Pauli, Richard M. "Achondroplasia: a comprehensive clinical review." <i>Orphanet Journal of Rare Diseases</i> 14: 1-49 (2019).
1007	Högler, Wolfgang, and Ward, Leanne M. "New developments in the management of achondroplasia." <i>Wiener Medizinische Wochenschrift</i> 170: 104-111 (2020).
1008	US Patent No 9,907,834 to Bullens et al., issued March 6, 2018
1009	Wendt, Daniel J., et al. "Neutral endopeptidase-resistant C-type natriuretic peptide variant represents a new therapeutic approach for treatment of fibroblast growth factor receptor 3-related dwarfism." <i>The Journal of Pharmacology and Experimental Therapeutics</i> 353: 132-149 (2015).
1010	Baujat, Geneviève, et al. "Achondroplasia." <i>Best Practice & Research Clinical Rheumatology</i> 22: 3-18 (2008).
1011	Ornitz, David M., and Marie, Pierre J. "FGF signaling pathways in endochondral and intramembranous bone development and human genetic disease." <i>Genes & Development</i> 16: 1446-1465 (2002).
1012	Ornitz, David M., and Legeai-Mallet, L. "Achondroplasia: development, pathogenesis, and therapy." <i>Developmental Dynamics</i> 246: 291-309 (2017).

Exhibit No.	Description
1013	Wallis, Gillian A. “Bone growth: coordinating chondrocyte differentiation.” <i>Current Biology</i> 6: 1577-1580 (1996).
1014	Su, Nan, et al. “FGF signaling: its role in bone development and human skeleton diseases.” <i>Frontiers in Bioscience</i> 13:2842-2865 (2008).
1015	Krakow, D. “Skeletal Dysplasias” <i>Clin Perinatol</i> 42: 301-319 (2015)
1016	Nguyen, Jie C., et al. “Imaging of pediatric growth plate disturbances.” <i>Radiographics</i> 37: 1791-1812 (2017).
1017	Yamanaka, Shigeki, et al. “Circulatory CNP rescues craniofacial hypoplasia in achondroplasia.” <i>Journal of Dental Research</i> 96: 1526-1534 (2017).
1018	Rimoin, David L., et al. “The Skeletal Dysplasias: Clinical–Molecular Correlations.” <i>Annals of the New York Academy of Sciences</i> 1117: 302-309 (2007).
1019	Krejci, Pavel, et al. “Interaction of fibroblast growth factor and C-natriuretic peptide signaling in regulation of chondrocyte proliferation and extracellular matrix homeostasis.” <i>Journal of Cell Science</i> 118: 5089-5100 (2005).
1020	Pejchalova, Katerina, et al. “C-natriuretic peptide: an important regulator of cartilage.” <i>Molecular Genetics and Metabolism</i> 92: 210-215 (2007).
1021	Wu, Chengliang, et al. “Furin-mediated processing of Pro-C-type natriuretic peptide.” <i>Journal of Biological Chemistry</i> 278: 25847-25852 (2003).
1022	Meyer, Markus, et al. “Chapter 58: Natriuretic peptides.” <i>Acute Heart Failure</i> : 608-620 (2008).
1023	U.S. Patent No. 8,198,242 to Wendt et al., issued June 12, 2012
1024	<i>Intentionally left blank</i>

Exhibit No.	Description
1025	Mortier, Geert R., et al. “Nosology and classification of genetic skeletal disorders: 2019 revision.” <i>American Journal of Medical Genetics Part A</i> 179: 2393-2419 (2019)
1026	Breinholt, Vibeke Miller, et al. “TransCon CNP, a sustained-release C-type natriuretic peptide prodrug, a potentially safe and efficacious new therapeutic modality for the treatment of comorbidities associated with fibroblast growth factor receptor 3–related skeletal dysplasias.” <i>The Journal of Pharmacology and Experimental Therapeutics</i> 370: 459-471 (2019).
1027	Merker, Andrea, et al. “Growth in achondroplasia: development of height, weight, head circumference, and body mass index in a European cohort.” <i>American Journal of Medical Genetics Part A</i> 176: 1723-1734 (2018).
1028	Reid, Cheryl S., et al. “Cervicomedullary compression in young patients with achondroplasia: value of comprehensive neurologic and respiratory evaluation.” <i>The Journal of Pediatrics</i> 110: 522-530 (1987).
1029	Hecht, Jacqueline T., et al. “Mortality in achondroplasia.” <i>American Journal of Human Genetics</i> 41: 454-464 (1987).
1030	Simmons, Kristen, et al. “Mortality in babies with achondroplasia: revisited.” <i>Birth Defects Research Part A: Clinical and Molecular Teratology</i> 100: 247-249 (2014).
1031	Bartels, Cynthia F., et al. “Mutations in the transmembrane natriuretic peptide receptor NPR-B impair skeletal growth and cause acromesomelic dysplasia, type Maroteaux.” <i>The American Journal of Human Genetics</i> 75: 27-34 (2004).
1032	Chitty, L. S., et al. “New aids for the non - invasive prenatal diagnosis of achondroplasia: dysmorphic features, charts of fetal size and molecular confirmation using cell - free fetal DNA in maternal plasma.” <i>Ultrasound in Obstetrics & Gynecology</i> 37: 283-289 (2011).

Exhibit No.	Description
1033	“General Clinical Pharmacology Consideration for Neonatal Studies for Drugs and Biological Products Guidance for Industry” U.S. Department of Health and Human Services, July 2019
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1035	Horton, William A., et al. “Achondroplasia.” <i>The Lancet</i> 370: 162-172 (2007).
1036	Bianchi, M. L. “Hypophosphatasia: an overview of the disease and its treatment.” <i>Osteoporosis International</i> 26: 2743-2757 (2015).
1037	McInerney-Leo, Aideen M., et al. “Short-rib polydactyly and Jeune syndromes are caused by mutations in WDR60.” <i>The American Journal of Human Genetics</i> 93: 515-523 (2013).
1038	Yasoda, Akihiro, and Nakao, Kazuwa. “Translational research of C-type natriuretic peptide (CNP) into skeletal dysplasias.” <i>Endocrine journal</i> 57: 659-666 (2010).
1039	Prickett, T. C., & Espiner, E. A. (2011). C-type natriuretic peptide (CNP) and postnatal linear growth. In <i>Handbook of growth and growth monitoring in health and disease</i> (pp. 2789-2809). New York, NY: Springer New York.
1040	Miura, Kohji, et al. “Overgrowth syndrome associated with a gain - of - function mutation of the natriuretic peptide receptor 2 (NPR2) gene” <i>American Journal of Medical Genetics Part A</i> 164: 156-163 (2013).
1041	European Patent 0769554 B1 to Tanaka et al., issued March 5, 2008
1042	Naski, Michael C., et al. “Repression of hedgehog signaling and BMP4 expression in growth plate cartilage by fibroblast growth factor receptor 3.” <i>Development</i> 125: 4977-4988 (1998).
1043	Bienaimé, Jean-Jacques “38 th Annual J.P. Morgan Healthcare Conference.” BioMarin. PowerPoint Presentation. January 2020.

Exhibit No.	Description
1044	Minina, Eleonora, et al. “Interaction of FGF, Ihh/Pthlh, and BMP signaling integrates chondrocyte proliferation and hypertrophic differentiation.” <i>Developmental Cell</i> 3: 439-449 (2002).
1045	Oefner, Christian, et al. “Structure of human neutral endopeptidase (Neprilysin) complexed with phosphoramidon.” <i>Journal of Molecular Biology</i> 296: 341-349 (2000).
1046	International Publication WO 2009/067639 (Wendt)
1047	Definition of “Mammal,” Merriam-Webster’s Collegiate Dictionary, 11 th Edition (2020).
1048	Definition of “Mammal,” Cambridge Advanced Learner’s Dictionary, 4 th Edition (2013).
1049	Watanabe, Yasuhiro, et al. “Comparison of the hydrolysis of the three types of natriuretic peptides by human kidney neutral endopeptidase 24.11.” <i>Biochemical and Molecular Medicine</i> 61: 47-51 (1997).
1050	Mora, Camilo, et al. “How many species are there on Earth and in the ocean?” <i>PLoS Biology</i> 9: e1001127 (2011).
1051	Shim, Kye Shik. “Pubertal growth and epiphyseal fusion.” <i>Annals of Pediatric Endocrinology & Metabolism</i> 20: 8-12 (2015).
1052	Excerpt from Nelson, D. L., and Cox, M. M. “Lehninger Principles of Biochemistry,” W. H. Freeman (2013)
1053	Long, Shinong, et al. “A novel method for the large-scale production of PG-CNP37, a C-type natriuretic peptide analogue.” <i>Journal of Biotechnology</i> 164: 196-201 (2012).
1054	Neumeyer, L., Merker, A., & Hagenäs, L. “Clinical charts for surveillance of growth and body proportion development in achondroplasia and examples of their use.” <i>American Journal of Medical Genetics Part A</i> 185: 401-412 (2021).

Exhibit No.	Description
1055	Hoover-Fong, Julie E., et al. “Achondroplasia Natural History Study (CLARITY): a multicenter retrospective cohort study of achondroplasia in the United States.” <i>Genetics in Medicine</i> 23: 1498-1505 (2021).
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1058	Burdan, F., et al., “Morphology and physiology of the epiphyseal growth plate,” <i>Folia Histochemica Et Cytobiologica</i> 47:5-16 (2009)
1059	Anderson, B. J., and Holford, N. H. G., “Understanding dosing: children are small adults, neonates are immature children.” <i>Archives of Disease in Childhood</i> 98:737-744 (2013).
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1061	Wiens, J. “Explaining large scale patterns of vertebrate diversity.” <i>Biology Letters</i> 11: 1-13 (2015).
1062	Espiner, E. et al. “Plasma C-Type Natriuretic Peptide: Emerging Applications in Disorders of Skeletal Growth.” <i>Hormone Research In Paediatrics</i> 90: 345-357 (2019).
1063	Lorget, F., et al. “Evaluation of the Therapeutic Potential of a CNP Analog in a Fgfr3 Mouse Model Recapitulating Achondroplasia 2012.” <i>The American Journal of Human Genetics</i> 97: 1108-1114 (2012).
1064	File History of U.S. Reissue Patent No. RE48,267, filed July 11, 2017
1065	Complaint for Patent Infringement, <i>BioMarin Pharma. Inc. v. Zydus Lifesciences Limited</i> , Case No. 1:26-cv-01005 (D.N.J.), filed February 2, 2026
1066	“Leadership,” Ascendis Pharma, accessible at https://ascendispharma.us/about-us/leadership/ (last accessed March 2, 2026)

Exhibit No.	Description
1067	“Corporate Executive Committee,” Bachem AG, accessible at https://www.bachem.com/about-bachem/company-overview/leadership/executive-committee/ (last accessed March 2, 2026)
1068	“The Executive Board,” Wacker Chemie AG, accessible at https://www.wacker.com/cms/en-us/about-wacker/profile-and-organization/executive-board.html (last accessed March 2, 2026)
1069	“Contact Us,” Ascendis Pharma, accessible at https://ascendispharma.com/contact-us/ (last accessed March 2, 2026)
1070	“Contact,” Bachem AG, accessible at https://www.bachem.com/contact/ (last accessed March 2, 2026)
1071	“Locations worldwide”, Wacker Chemie AG, accessible at https://www.wacker.com/cms/en-us/global-contents/map/map-page.html (last accessed March 3, 2026)
1072	Time Milestones for the Federal District Court of the District of New Jersey, Docket Navigator Report generated March 3, 2026 (annotated)

I. INTRODUCTION

The Director should assess the merits of the Petition and institute this PGR. During examination, Patent Owner (PO) misled the Examiner into making several material errors, resulting in a patent that should never have issued. It is undisputed that well before the '106 patent's claimed priority date, the art taught a method of treating skeletal dysplasia in children 5 years old by administering a composition comprising a "C-type natriuretic peptide (CNP) variant" known as vosoritide. The '106 patent claims an obvious variation of this prior art method: a method of treating skeletal dysplasia in a "subject" "about 0 month to about 2 years old" by administering a composition comprising a CNP variant. The Examiner misapprehended several aspects of the claims during examination, resulting in material errors. For example, the Examiner failed to appreciate the claims' enormous scope that encompasses treating hundreds of different types of skeletal dysplasias in thousands of different animal species using a diverse library of CNP variants. The '106 patent's limited specification does not enable this massive scope. The Examiner also failed to identify anticipatory prior art, and erred in assessing a skilled artisan's reasonable expectation of success. The merits of the Petition are strong, addressing each of these issues with detailed evidence and argument. The Director should institute this PGR so the Board can correct the Office's errors and cancel the challenged claims.

II. DISCRETIONARY DENIAL IS NOT WARRANTED.

A. Petitioner’s proposed construction different from an unrelated ITC proceeding is warranted.

Under *Revvo Techs., Inc. v. Cerebrum Sensor Tech., Inc.*, IPR2025-00632, Paper 20 at 5 (Squires Nov. 3, 2025) (precedential), petitioners must “explain sufficiently” why different claim construction positions between the PTAB and another forum are warranted. Petitioner did not need to explain differences between this PGR and an ITC proceeding because: (i) the ’106 patent is not involved in the ITC proceeding, nor is it related to the patent asserted in the ITC; (ii) claims of such unrelated patents must be construed separately; and (iii) even if comparing Petitioner’s claim construction positions in the two proceedings (for two different patents), Petitioner has *not* proposed inconsistent constructions.

1. The RE’267 patent involved in the ITC proceeding is unrelated to the ’106 patent involved in this PGR.

PO’s attempt to draw similarities between this PGR and the ITC proceeding directly contradicts PO’s admission in the mandatory notices. Rule 42.8(b)(2) requires parties to “[i]dentify any other judicial or administrative matter that would affect, or be affected by, a decision in the proceeding.” 37 C.F.R. § 42.8(b)(2). PO stated in its mandatory notices for this PGR that there are *no related matters*. Paper 5 at 1 (“*Patent Owner identifies no matters that may be deemed related pursuant to*

37 C.F.R. § 42.8(b)(2).”).¹ Thus, according to PO, the ITC proceeding (which does not involve the ’106 patent) is unrelated to this PGR and would not affect, or be affected by, a decision in this PGR.

This makes sense, because the RE’267 and ’106 patents have no formal relationship. There is no relation by priority, as the two patents claim priority dates that are *over 12 years apart*. *Compare* EX2004, face (May 20, 2009, priority claim) *with* EX1001, face (July 9, 2021, priority claim). There is no overlap in inventorship. *Compare* EX2004, face and p. 209 (listing inventors Wendt, Long, Castillo, Price, Aoyagi-Scharber, Vellard, Okhamafe, Bell, and Bliesath) *with* EX1001, face (listing inventors Day and Fischeleva). The specifications (“the single best guide to the meaning of a disputed term”) and claims are substantively different. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (en banc) (internal quotations omitted). For example, the RE’267 patent specification includes 83 Figures, 19 Examples, and 237 sequences, while the ’106 patent includes only four Figures, a single Example, and 68 sequences. The two patents also claim different Markush groups of CNP variants. *Compare* EX2004, claim 15, *with* EX1001, claim 1. The file histories of the two patents are also different. *Compare* EX1002 *with* EX1064. In sum, “the [’106 patent] was not filed as a

¹ Emphasis has been added throughout, unless otherwise noted.

continuation, continuation-in-part, or divisional application of the [RE267 patent].

These [patents] have no formal relationship and were presented to the patent office as patentably distinct inventions.” *Abbott Lab ’ys v. Dey, L.P.*, 287 F.3d 1097, 1104-1105 (Fed. Cir. 2002). Accordingly, there are not “different claim constructions” at play here, as there were in *Revvo* and *Tesla*. *Revvo*, Paper 20; *Tesla, Inc. v. Intellectual Ventures II LLC*, IPR2025-00340, Paper 18 (Squires Nov. 5, 2025) (informative).

2. Claims of unrelated patents must be construed separately.

PO ignores “the well-understood notion that claims of unrelated patents must be construed separately.” *eDigital Corp v. Futurewei Techs., Inc.*, 772 F.3d 723, 726-727 (Fed. Cir. 2014); *see also Pfizer, Inc. v. Ranbaxy Lab ’ys Ltd.*, 457 F.3d 1284, 1290 (Fed. Cir. 2006); *Abbott Lab ’ys*, 287 F.3d at 1104; *Commonwealth Sci. v. BASF Plant Sci. Co. GmbH*, PGR2020-00057, Paper 9 at 12 (P.T.A.B. Oct. 15, 2020). Thus, there was no need for Petitioner to explain a different claim construction position for an unrelated patent in an unrelated proceeding. *Id.*; Paper 5 at 1.

In *Revvo* and *Tesla*, the petitioner advanced different claim construction positions for the *same term(s) in the same patent* in different forums, without explaining the why the differences were warranted. *Revvo*, Paper 20 at 2; *Tesla*, Paper 18 at 4; *see also Sun Pharms. Indus. Inc. v. Nivagen Pharms., Inc.*, IPR2025-

00893, Paper 18 (Stewart Sept. 19, 2025) (informative); *Infinion Techs. Americas Corp. v. Mosaid Techs. Inc.*, IPR2025-01171, Paper 27 at 3 (Squires Feb. 19, 2026); *Carbyne, Inc. v. Tritech Software Sys.*, IPR2025-00959, Paper 20 at 4 (Squires Feb. 19, 2026). These Director and Board decisions are distinguishable, because the '106 patent and RE'267 patent have “no formal relationship” and are separated by over 12 years in priority claims. *Abbott Lab'ys*, 287 F.3d at 1104-1105; *see also Generac Power Sys., Inc. v. Champion Power Equipment, Inc.*, IPR2025-00805, Paper 40 at 4 (Squires Feb. 3, 2026) (Director finding that the IPR-challenged patent not asserted in district court litigation was “related” to the “patents that are asserted,” confirmed in the patent owner’s mandatory notices). PO cites no authority requiring Petitioner to apply the same construction or explain different constructions for two unrelated patents in two unrelated proceedings. Moreover, as discussed below in Section II.A.3, Petitioner’s constructions of “CNP variant” here and at the ITC are *not* inconsistent.

3. Petitioner’s claim construction positions are consistent.

Even without any formal relationship between the RE'267 and '106 patents, Petitioner’s proposed constructions for the two patents are consistent. The ordinary and customary meaning is assessed “as of the effective filing date of the patent application.” *Phillips*, 415 F.3d at 1312. In view of the '106 patent claim language, specification, and file history, the ordinary and customary meaning of “CNP

variant” as of July 9, 2021, would have been understood to be a CNP variant “capable of binding to and activating NPR-B, and thereby inducing cGMP production.” DD Br., 1. The claim language “a *method of treating* skeletal dysplasia” in the ’106 patent conveys that the CNP variants are biologically active (i.e., they bind to and activate NPR-B, inducing cGMP production), as they must be administered in “an amount *effective to treat* the skeletal dysplasia in the subject.” EX1001, claim 1. The specification confirms this, stating that CNP variants have “substantially the *same or better biological activity* than wild-type CNP-22” and that they “*interact[] with NPR-B (GC-B) to stimulate the generation of cGMP.*” EX1001, 11:41-48; *see also, id.*, 12:37-47 (stating that CNP variant peptides “*retain CNP activity,*” shown as “retention of ... the *cGMP stimulating activity* of CNP-22....”).

The Petition applies this ordinary and customary meaning by relying on prior art that teaches CNP variants such as vosoritide are capable of binding to and activating NPR-B, and thereby inducing cGMP production. *See, e.g.,* Pet., 3 (explaining “CNP variants like vosoritide were developed to inhibit the constitutively active FGFR3 signal” by binding to the NPR-B receptor), 15 (“upon binding to its cellular receptor NPR-B CNP causes bone growth by inhibiting FGFR3 signaling” and including Figure 10 from EX1019, depicting CNP binding to and activating NPR-B, inducing cGMP production); *see also* EX1005, 32

(“Dose-dependent *increases in urinary cGMP* ... were observed ... suggest[ing] that the *pharmacologic activity of vosoritide* is sustained over the course of treatment.”); EX1007, FIG. 1 (depicting vosoritide as a molecule that binds and activates NPR-B, inducing cGMP production); EX1006, 41 (“increasing CNP activity [via CNP variants] could counteract the excess negative signal of *FGFR3* mutations” via NPR-B activation and cGMP production); EX1008, 6:53-60 (“CNP variant peptides ... may have greater activity than CNP22, e.g., with respect to *interaction with NPR-B* (GC-B) to stimulate the *generation of cGMP*.”); EX1023, 22:57-61 (same), 69:58-61 (“the CNP variants retain ... the *cGMP-stimulation activity* of wild-type CNP22....”). PO has not disputed that vosoritide is capable of binding to and activating NPR-B, and thereby inducing cGMP production. Accordingly, Petitioner’s positions before the ITC and PTAB are consistent, notwithstanding that they involve unrelated patents filed 12 years apart. *Revvo*, Paper 20 at 5; *Tesla*, Paper 18 at 4.

B. None of the *Fintiv* factors supports denial.

If instituted, this PGR will conclude well before any district court trial date. District court litigation involving the ’106 patent, which does not involve the same parties as here, has barely begun. PO asserted the ’106 patent in the U.S. District Court of New Jersey against an unrelated third party, Zydus Lifesciences, Ltd., on February 2, 2026, purportedly in response to Zydus’s Abbreviated New Drug

Application (ANDA) to the FDA. EX1065, ¶¶1, 40. Citing no evidence, PO speculates that “validity [of the ’106 patent] will be litigated and adjudicated in parallel.” DD. Br., 19. The evidence shows otherwise. If instituted, the Board would issue a Final Written Decision in this PGR by approximately June 2027. The median time to trial in ANDA cases in the District of New Jersey is about 34 months, setting an estimated trial date for PO’s *Zydu*s litigation in *December 2028*—over one year after completion of this PGR. EX1072 (showing median of 34.1 months and average of 39.4 months for bench trials in ANDA cases terminated on or after Jan. 1, 2023). Moreover, is not even clear what invalidity arguments *Zydu*s may raise in district court. None of the *Fintiv* factors supports denial. *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 at 6 (P.T.A.B. Mar. 20, 2020) (precedential).

C. The Petition identifies all real parties in interest in this PGR.

1. Neither Bachem nor Wacker control or fund this PGR.

Neither Bachem nor Wacker “exercised or could have exercised control over [Petitioner’s] participation in [this PGR],” and neither entity “funds and directs and controls” this PGR. *Corning Optical Comms. RF, LLC v. PPC Broadband, Inc.*, IPR2014-00440, Paper 68 at 14 (P.T.A.B. Aug. 18, 2015) (designated precedential Oct. 28, 2025). “[T]he evidence as a whole must show that the non-party possessed effective control over the [PGR] proceeding.” *Id.*, 15. PO provides no evidence

showing Bachem or Wacker controls or funds this PGR. Indeed, neither company is involved in the PGR at all.

2. Bachem and Wacker’s supplier or manufacturer relationship does not make them RPIs.

“A patent owner challenging a petitioner’s RPI disclosure must provide sufficient evidence to show the disclosure is inadequate.” *Corning*, Paper 68 at 13. PO’s only “evidence” is that Bachem and Wacker are the supplier and manufacturer of Petitioner’s TransCon CNP product and are co-respondents with Petitioner in the ITC proceeding involving the unrelated RE’267 patent. DD Br., 8; EX2005, ¶24; Paper 5, 1. But “[a] party does not become a RPI merely through association with another party in an endeavor unrelated to the [PGR] proceeding.” *Corning*, Paper 68 at 14. Even assuming TransCon CNP were related to this PGR, merely being a supplier or manufacturer does not make Bachem or Wacker RPIs here. *See, e.g., WesternGeco LLC v. ION Geophys. Corp.*, 889 F.3d 1308, 1321 (Fed. Cir. 2018) (discussing “customer-manufacturer relationship”); *Toshiba Memory Corp. v. Anza Tech., Inc.*, IPR2018-01597, Paper 56 at 15 (P.T.A.B. Mar. 12, 2020) (discussing “customer-supplier relationships”); *Shenzhen Ronglida Tech. Co. Ltd. v. Pathway IP LLC*, IPR2025-01231, Paper 12 at 9 (P.T.A.B. Jan. 15, 2026) (discussing “shared supply chain”). Likewise, Bachem’s and Wacker’s status as co-respondents in the ITC proceeding is insufficient for RPI status. *See, e.g., Denso Corp. v. Beacon Navigation GmbH*, IPR2013-00026, Paper 34 at 10–

11 (P.T.A.B. Mar. 14, 2014) (“The mere fact that parties are co-defendants or concurrent defendants in litigation does not make them [RPIs].”); Office Trial Practice Guide at 17 (similar).

3. There are no blurred lines of corporate separation.

Bachem, Wacker, and Petitioner “are distinct and unrelated corporate entities represented by different counsel.” *WesternGeco*, 889 F.3d at 1320. Each company is represented by different counsel before the ITC and they do not have an overlap in executive leadership. *See, e.g.*, EX2005, 36-37; EX2006, Appx. A, 6-10; EX2011, 21-22; EX1066; EX1067; EX1068. Each company maintains separate and distinct physical locations. *See* EX1069; EX1070; EX1071. Thus, there are no blurred “lines of corporate separation” between Petitioner, Bachem, and Wacker. *Corning*, Paper 68 at 16; *see also Galderma S.A. v. Allergan Industrie, SAS*, IPR2014-01422, Paper 14 (P.T.A.B. Mar. 5, 2015); *Zoll Lifecor Corp. v. Philips Elecs. N. Am. Corp.*, IPR2013-00606, Paper 13 at 10 (P.T.A.B. Mar. 20, 2014). And there is no question as to Petitioner’s “actual identity.” *See Yangtze Memory Techs. Co., Ltd. v. Micron Tech., Inc.*, IPR2025-00098, Paper 38 at 6-7 (Squires Jan. 15, 2026) (informative).

4. Patent Owner can only speculate that Bachem or Wacker would benefit from this PGR.

PO speculates that Wacker and Bachem would benefit from this PGR because it “reduc[es] BioMarin’s U.S. patent protection constraining the same

accused product and supply chain.” DD Br., 9. PO’s argument is baseless. The “accused product” is Petitioner’s TransCon CNP, which PO accuses of infringing *the RE’267 patent*, not the ’106 patent. EX2005; EX1007, 108. *See Ventex Co., Ltd. v. Columbia Sportswear N. Amer., Inc.*, IPR2017-00651, Paper 148 at 10 (P.T.A.B., Jan. 24, 2019)² (precedential) (cautioning “not to overextend the reasoning ... to any situation where a party benefits generally from the filing of the Petition and also has a relationship with the Petitioner”) (internal quotes omitted).

In sum, the Petition identifies *all* RPIs. 35 U.S.C. § 322(a)(2).

D. The Petition satisfies *Advanced Bionics*.

The Petition presents combinations of art and arguments that are not the same or substantially the same as those previously presented to the Office, satisfying step (1) in *Advanced Bionics, LLC v. Med-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (P.T.A.B. Feb. 13, 2020) (precedential). The Examiner also made multiple material errors, satisfying *Advanced Bionics* step (2). *Id.*

² In *Ventex*, a supplier / manufacturer was a defendant in related litigation involving the IPR-challenged patent, and both petitioner and patent owner in the IPR identified the related litigation in their mandatory notices. *Id.* at 4, 8-9.

1. The Petition presents new art and arguments not previously presented to the Office (*Advanced Bionics* step (1)).

Grounds 1-4 (obviousness) present *new* art combinations and *new* and detailed arguments on reasonable expectation of success—evidence and argument missing during prosecution. Grounds 5 (anticipation), 6 (enablement), and 7 (improper claim) also present new arguments not previously before the Office.

a. Högler and Pauli are not cumulative of the art considered by the Examiner.

There is no dispute that PO did not provide Högler or Pauli to the Office during examination. Pet., 8, 23; DD Br., 11-12. Thus, the base combinations of *Högler* and Savarirayan (Grounds 1-2) and *Pauli* and Savarirayan (Grounds 3-4) were likewise not previously presented to the Office. PO also does not dispute this. Instead, PO argues that each of Högler and Pauli is “cumulative” of the art applied by the Examiner and that neither reference “adds [] *completed infant efficacy* data bearing on reasonable expectation of success.” DD Br., 12-13. PO is wrong on the law and the facts.

First, PO presents a myopic view of Högler’s and Pauli’s teachings as limited to the “same clinical studies” in Savarirayan and the “ideal” age range for treating achondroplasia, respectively. DD Br., 11-12. But the Petition shows that Högler and Pauli each teaches far more than these disclosures cherry-picked by PO. *See, e.g.*, Pet., 34-36 (discussing Högler’s teachings of FGFR3 mutations,

foramen magnum and spinal stenosis, and chondrocyte proliferation), 54-56

(discussing Pauli's teachings of FGFR3 mutations, chondrocytic bone growth, and cartilaginous bone growth). Höglér and Pauli are not cumulative with the Examiner's art.

Second, PO's demand for "*completed* infant efficacy data" in Höglér and Pauli is contrary to the law of obviousness, which does not require "[c]onclusive proof of efficacy" or "absolute predictability of success." *Hoffmann-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1331 (Fed. Cir. 2014); *OSI Pharm., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019). PO's argument is also misleading as it implies that the claims are limited to *human* "infants," which is wrong. Pet., 23-24, 75-76. The claims recite only the term, "subject," which encompasses "mammals and non-mammals." *Id.*; EX1001, 63:36-67:60.

b. The Petition presents new arguments not previously presented to the Office.

Grounds 1-4. During prosecution, PO argued that a skilled artisan would not have had a reasonable expectation of successfully practicing the claimed method because the Examiner's cited art "only discloses the effects of CNP therapy in children over 5 years old." EX1002, 0935-0937. The Petition presents new arguments and evidence demonstrating a reasonable expectation of success in treating subjects 0 months to 2 years of age—including express disclosures from

Högler, Pauli, and Savarirayan together with knowledge in the art (e.g., Yamanaka, EX1017) that were missed during examination. Pet., 33-37, 54-56.

Specifically, the Petition presents new arguments regarding the *underlying mechanism* behind achondroplasia and a skilled artisan's corresponding expectations, as well as evidence of CNP successfully rescuing foramen magnum stenosis in "subjects" less than two years old—teachings missed by the Examiner that would have informed a skilled artisan's reasonable expectations of success. For example, as the Petition explains, Högler teaches that the "heterozygous, activating mutation in fibroblast growth factor receptor-3 (FGFR3) gene" activates a MAPK signaling pathway that "puts a continuous permanent break onto chondrocyte proliferation in all growth plates...." EX1007, Abstract, 105; Pet., 34; EX1003, ¶¶77, 82-83. The Petition also explains that Pauli teaches that "nearly all instances of achondroplasia are caused by FGFR3 mutations," and that FGFR3 is a "negative regulator" of chondrocytic bone growth. EX1006, 3; Pet., 54-55. The Petition further explains that CNP variants (e.g., vosoritide) were known to "treat achondroplasia and its symptoms by counteracting the FGFR3 activation" (Pet., 34, 55) and CNP "successfully rescued achondroplasia complications, such as foramen magnum stenosis" in young mice (subjects) less than 12-weeks old. Pet., 36, 56; EX1017, Abstract, 1532, FIG. 4. The Petition also explains how "CNP signaling was important for bone growth in 0-2 year old children with

achondroplasia.” Pet., 35-36; EX1031, 27. This evidence—directly relevant to a reasonable expectation of success—was either not submitted to the Office at all or missed by the Examiner. EX1002, 0906-0910.

Ground 5 (anticipation) presents a new argument not previously presented to the Office because the Examiner erred in failing to identify Wendt-242 as anticipatory art. Pet., 63-74. **Ground 6** (enablement) also presents a new argument because the Examiner never raised any enablement rejections under § 112(a). And while examiners *should* assess patent applications for complying with § 112(a), the Examiner here clearly did not understand the full scope of the claims. Nothing in the record indicates the Examiner considered the enablement deficiencies discussed in the Petition or claim 1’s scope at all. EX1002, 0904-0906; Pet., 74-87. **Ground 7** (improper claim) also presents new arguments. The Examiner initially rejected original claim 14 (now issued claim 8) for failing to further limit the claim from which it depends, but PO subsequently amended the claims to change the antecedent basis. EX1002, 0905, 0924. Ground 7 presents a new argument under § 112(d) (i) addressing PO’s new claim language and (ii) explaining how claim 8 contradicts claim 5. Pet., 87-89.

2. The Examiner materially erred (*Advanced Bionics* step (2)).

Advanced Bionics step (2) is satisfied because the Examiner materially erred. *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 5-6

(Stewart May 19, 2025) (precedential).

With respect to **Grounds 1-4**, the Examiner erred in finding no reasonable expectation of success because she failed to consider the underlying pathophysiology of achondroplasia and its complication, foramen magnum stenosis, such as *FGFR3* mutations and constitutively active signaling in subjects 0-2 years old, and CNP's ability to mitigate it. The Petition demonstrates a reasonable expectation of success by providing the missing evidence and explanation, all of which is supported by expert testimony. Pet., 33-37, 54-56; EX1003, ¶¶81-92, 131-136; Section II.D.1.b. The Examiner's error is further evident from her search strategies, which focused on CNP amino acid sequences, inventor and assignee names, and terms such as "skeletal dysplasia," "achondroplasia," "CNP," "Pro-Gly-CNP37," "0 to 2 years old," and "infants." Her search terms did not include, e.g., "FGFR3" or "foramen magnum stenosis." See e.g., EX1002, 0882-0887, 0946, 0948-0954.

Moreover, the Examiner's conclusion regarding lack of predictability was not based on any evidence. PO provided *no evidence* of unpredictability in treating a subject 0-2 years old, while arguing that a skilled artisan would not have predicted success. EX1002, 0936-0937. Nothing has changed. DD Br., 15. PO argues that infants with achondroplasia can have severe and fatal respiratory complications due to foramen magnum stenosis. *Id.* But these complications are

motivation to treat the subjects, not evidence of unpredictability of *treating* them with CNP. Pet., 30-37, 51-56. PO argues that Savarirayan’s study of vosoritide’s “safety and side effect profile” somehow evidences uncertainty in the field. DD Br., 15. PO ignores Savarirayan’s conclusions that vosoritide is not only safe but *effective*. See e.g., EX1005, Abstract. Moreover, PO itself publicly disclosed in 2020 that vosoritide’s “safety and tolerability *in infants* and children” was generally consistent with the safety profile of the Phase II vosoritide clinical trial that resulted in drug approval. EX1043, 26; Pet., 19.

Second, with respect to **Ground 5**, the Examiner erred in failing to recognize that Wendt-242 (EX1023) is anticipatory prior art. Pet., 63-74. PO argues that Example 13 of Wendt-242 “relates to mice studies as opposed to *studies in infants, as claimed*.” DD Br., 16. The challenged claims, however, recite treating a “subject” (not “infants”), and the term “subject” in the ’106 patent encompasses mice. EX1001, 18:55-65, claim 1; Pet., 75-76; EX1003, ¶¶52, 182. On this basis alone, the Petition showed that Wendt-242 anticipates the challenged claims. Pet., 63-74. It is not surprising that the Examiner erred regarding Wendt-242’s disclosures, because PO used similarly misleading arguments during prosecution. See EX1002, 0935-0936 (arguing that “the claims are directed to treatment of *skeletal dysplasia patients*”; discussing “treatment of the *patient population* in the claims”; and “[t]he efficacy of the treatment in the selected

patient population.”). And in her Reasons for Allowance, the Examiner discussed predicting “results in *children.*” EX1002, 0966. The Examiner did not appreciate that the claims encompass treating *mice* (or *any other mammal*) as “subjects” of the ’106 patent, resulting at least in part in her failure to identify Wendt-242 as anticipatory art. PO also argues that Wendt-242’s Example 19 purportedly has “the same relevant disclosures as Example 12 in Wendt-639” asserted by the Examiner. DD Br., 16-17. But the Examiner raised an *obviousness* rejection over Wendt-639 and Bullens, not anticipation. EX1002, 0906-0910. Anticipation does not require a reasonable expectation of success. *See e.g., Agilent Tech., Inc. v. Synthego Corp.*, 139 F.4th 1319, 1327 (Fed. Cir. 2025) (“anticipation does not require the actual creation or reduction to practice of the prior art subject matter.”).

Third, with respect to **Grounds 6-7**, the Examiner failed to appreciate the full scope of the claims. As discussed above, the term “subject” in claim 1 is *not* limited to human infants—it encompasses thousands of animal species. The claim terms “CNP variant” and “skeletal dysplasia” extend this scope even further, encompassing treatment of over 450 different skeletal dysplasias, in thousands of different animal species, using over 65 different CNP variants. Pet., 75-83. The Examiner erred in failing to recognize this massive claim scope, which is not enabled by the narrow specification. Pet., 74-87.

E. Patent Owner has no settled expectations for the ’106 patent.

The '106 patent issued February 25, 2025; the Petition was filed November 24, 2025. “Early challenges favor robust, predictable patent rights and weigh against discretionary denial.” *Straumann USA, LLC v. Smart Denture Conversions, LLC*, PGR2025-00054, Paper 11 at 2 (Stewart Oct. 17, 2025). Indeed, “petitions for [PGR] are favored because they must be filed no later than nine months from the grant of the patent..., are close in time to examination, and occur before expectations in the patent rights are strongly settled.” *Id.*

F. The merits of the Petition are strong.

The Petition’s merits are strong and fully supported by record evidence. During prosecution, PO admitted that the prior art *suggests* practicing the claimed method. *See, e.g.*, EX1002, 0936 (“Wendt generally discloses that younger children suffering from achondroplasia *could* benefit from treatment with CNP.” (emphasis in original)). PO’s only hook for allowance was its misleading argument that the field was unpredictable and there was no proof of efficacy. *Id.*, 0935-0937. **Grounds 1-4** set the record straight, providing detailed explanations and evidence demonstrating, among other aspects, pathophysiological basis for a reasonable expectation of success. Pet., 25-63. **Ground 5** provides a detailed, claim-by-claim analysis demonstrating that Wendt-242 anticipates the challenged claims. Pet., 63-74. **Ground 6** (enablement) addresses the claims’ massive scope, explaining that the claims cover “treating” hundreds of different types of skeletal dysplasia in

thousands of animal species using a library of diverse CNP variants, while the specification provides scant guidance and only a single example. Pet., 83-87. And **Ground 7** further details how claim 8 is unpatentable under § 112(d), due to (i) reciting optional language; and (ii) contradicting claim 5. Pet., 87-89.

G. No other considerations apply here.

In its argument for “efficiency and finality,” PO wrongly mischaracterizes the Petition’s arguments as being “repackage[d]” issues. DD Br., 19. As discussed above, the unpatentability arguments in Ground 5 (§ 102) and Grounds 6-7 (§ 112) were *never presented to the Office*. And Grounds 1-4 (§ 103) present new combinations of art with new evidence and rationales evincing a reasonable expectation of success. This is not repackaging; this is evidence and argument that were missing during prosecution. *Zuhai CosMX Battery Co., Ltd. v. Ningde Amperex Tech. Ltd.*, IPR2025-00405, Paper 24 (Squires Oct. 15, 2025), does not support PO’s argument. In *Zhuhai*, the Petition included “at least *fifteen grounds*,” several of which were not “sufficiently developed.” *Id.*, at 2-3. Here, all six of the Petition’s grounds are fully developed with reasoned argument and analysis.

III. CONCLUSION

Discretionary denial is not warranted. The Director should assess the merits of the Petition and institute trial.

Respectfully submitted,

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CERTIFICATE OF SERVICE (37 C.F.R. § 42.6(e))

I certify that the above-captioned **PETITIONER'S BRIEF OPPOSING
DISCRETIONARY DENIAL** and associated Exhibits 1064-1072 were served in
their entireties on March 3, 2026, upon the following parties via electronic mail:

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