

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Padagis US LLC,
Petitioner

v.

Neurelis, Inc.,
Patent Owner

Case No. IPR2025-00464
Patent No. 8,895,546

PATENT OWNER'S SUR-REPLY

TABLE OF CONTENTS

TABLE OF CONTENTS	i
TABLE OF AUTHORITIES	ii
TABLE OF EXHIBITS.....	iv
I. COLLATERAL ESTOPPEL DOES NOT APPLY	1
A. Issues Materially Differ.....	2
B. Issues Were Not Actually Litigated	4
1. Non-Obviousness over Gwozdz-PCT and Meezan	4
2. Priority of Gwozdz-PCT	5
II. PETITIONER CONFLATES §103(c) PROVISIONS	6
III. GWOZDZ-PCT IS NOT PRIOR ART	6
IV. THE CHALLENGED CLAIMS ARE NOT OBVIOUS	8
A. Failure to Disclose or Suggest All Claim Limitations	8
a. Petitioner’s Improper Claim Construction Tactics.....	9
b. Petitioner Shifts to New Theories in Reply	10
c. No Motivation to Combine	11
B. Petitioner’s Generic Motivations Do Not Establish Obviousness	13
1. Gwozdz-PCT Solves the Problem of Bioavailability	13
2. Gwozdz-PCT Solves the Problem of Solubility	14
3. The Combination Does Not Improve Stability	14
C. Petitioner’s Reliance on “Other Pharmaceutically Acceptable Additives” and “Wetting Agents”	17
D. Meezan Is Directed To Macromolecules and Does Not Address Compatibility with Tocopherol Solutions.....	17
E. No Motivation Toward Dodecyl Maltoside	18
V. CONCLUSION.....	20
CERTIFICATION OF WORD COUNT	21
CERTIFICATE OF SERVICE	22

TABLE OF AUTHORITIES

	Page(s)
Cases	
<i>ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.</i> , 694 F.3d 1312 (Fed. Cir. 2012).....	13
<i>Apple Inc. v. Andrea Elecs. Corp.</i> , 949 F.3d 697 (Fed. Cir. 2020).....	8
<i>Ariosa Diagnostics v. Verinata Health, Inc.</i> , 805 F.3d 1359 (Fed. Cir. 2015).....	11
<i>Belden Inc. v. Berk-Tek LLC</i> , 805 F.3d 1064 (Fed. Cir. 2015).....	3
<i>Comair Rotron, Inc. v. Nippon Densan Corp.</i> , 49 F.3d 1535 (Fed. Cir. 1995).....	2
<i>Google v. Hammond Development Int'l, Inc.</i> , 54 F.4th 1377 (Fed. Cir. 2022)	4
<i>Harmonic Inc. v. Avid Tech., Inc.</i> , 815 F.3d 1356 (Fed. Cir. 2016).....	8
<i>In re Fine</i> , 837 F.2d 1071 (Fed. Cir. 1998).....	12
<i>In re Fulton</i> , 391 F.3d 1195 (Fed. Cir. 2004).....	12, 19
<i>In re Riggs</i> , 131 F.4th 1377 (Fed. Cir. 2025)	5, 6
<i>KSR Int'l Co. v. Teleflex Inc.</i> , 550 U.S. 398 (2007).....	16
<i>MaxLinear, Inc. v. CF CRESPE LLC</i> , 880 F.3d 1373 (Fed. Cir. 2018).....	2
<i>Medtronic, Inc. v. Teleflex Innovations S.a.r.l.</i> , 69 F.4th 1341 (Fed. Cir. 2023)	15
<i>Millenium Pharms., Inc. v. Sandoz Inc.</i> , 862 F.3d 1356 (Fed. Cir. 2017).....	1

<i>Ohio Willow Wood Co. v. Alps South, LLC</i> , 735 F.3d 1333 (Fed. Cir. 2013).....	3
<i>Otsuka Pharm. Co., Ltd. v. Sandoz, Inc.</i> , 678 F.3d 1280 (Fed. Cir. 2012).....	1
<i>ParkerVision, Inc. v. Qualcomm Inc.</i> , 116 F.4th 1345 (Fed. Cir. 2024)	2
<i>Pers. Web Techs., LLC v. Apple, Inc.</i> , 848 F.3d 987 (Fed. Cir. 2017).....	13
<i>Pfizer, Inc. v. Apotex, Inc.</i> , 480 F.3d 1348 (Fed. Cir. 2007).....	16
<i>Purdue Pharma L.P. v. Depomed, Inc.</i> , No. 2015-2029, 643 F. App’x 960 (Fed. Cir. 2010).....	14
<i>Purdue Pharma L.P. v. Iancu</i> , No. 2018-1710, 767 F. App’x 918 (Fed. Cir. 2019).....	4, 5
<i>Revvo Techs., Inc. v. Cerebrum Sensor Techs., Inc.</i> , IPR2025-00632, Paper 20 (P.T.A.B. Nov. 3, 2025) (precedential).....	9, 10
<i>Soverain Software LLC v. Victoria’s Secret Direct Brand Mtmnt., LLC</i> , 778 F.3d 1311 (Fed. Cir. 2015).....	3
<i>Tesla, Inc. v. Intellectual Ventures II LLC</i> , IPR2025-00340, Paper 18 (P.T.A.B. Nov. 5, 2025) (informative).....	10
<i>TQ Delta, LLC v. 2Wire, Inc.</i> , No. 13-1835-RGA, 2021 WL 2671296 (D. Del. June 29, 2021)	4
<i>Uber Techs., Inc. v. X One, Inc.</i> , 957 F.3d 1334 (Fed. Cir. 2020).....	19
<i>Virtek Vision Int’l ULC v. Assembly Guidance Sys., Inc.</i> , 97 F.4th 882 (Fed. Cir. 2024)	16
Statutes	
35 U.S.C. §103(c) (pre-AIA)	6
Regulations	
37 C.F.R. §42.104(b)(3).....	10

TABLE OF EXHIBITS

Exhibit	Description of Exhibits
2001	Clinical Superiority Findings, U.S. Food & Drug Admin. (Dec. 18, 2024) https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings
2002	Scheduling Order entered in Neurelis, Inc. v. Padagis LLC, 1:24-cv-00562, D.I. 20 (D. Del. Aug. 28, 2024)
2003	Preliminary Invalidity Contentions served in Neurelis, Inc. v. Padagis LLC, 1:24-cv-00562 (D. Del. Dec. 20, 2024)
2004	Markman Order entered in Gilead Sciences, Inc. v. Lupin Ltd., 1:22-cv-00615-MN, D.I. 280 (D. Del. Feb. 21, 2025)
2005	Markman Order entered in Spinal Generations, LLC v. Depuy Synthes, Inc., 1:22-cv-01368 (MN), D.I. 147 (D. Del. Oct. 16, 2024)
2006	Orange Book Listing for U.S. Patent No. 8,895,546
2007	Declaration of Nicholas A. Peppas, Sc.D., dated December 6, 2018 in Aquestive Therapeutics, Inc. v. Hale Biopharma Ventures, LLC, IPR2019-00451, Exhibit 1041 (Jan. 29, 2019)
2008	Declaration of Daniel P. Wermeling, Pharm.D., dated January 27, 2020 in Aquestive Therapeutics, Inc. v. Hale Biopharma Ventures, LLC, IPR2019-00451, Exhibit 1150 (Jan. 28, 2020)
2009	NOT USED
2010	NOT USED
2011	NOT USED
2012	NOT USED

Exhibit	Description of Exhibits
2013	Scheduling Oral Order entered in Neurelis, Inc. v. Padagis LLC, 1:24-cv-00562, D.I. 47 (D. Del. March 11, 2025) Order Granting Stipulation to Extend Certain Fact Discovery Deadlines entered in Neurelis, Inc. v. Padagis LLC, 1:24-cv-00562, D.I. 65 (D. Del. May 15, 2025)
2014	Jacqueline A. French, Timothy A. Pedley, Initial Management of Epilepsy, New England Journal of Medicine 2008; 359:166-76 (“French & Pedley 2008”)
2015	Penovich et al., Burden of Seizure Clusters on Patients With Epilepsy and Caregivers, The Neurologist 2017; 22: 207-214
2016	Cloyd et al., Overcoming the Challenges of Developing an Intranasal Diazepam Rescue Therapy for the Treatment of Seizure Clusters, Epilepsia 2021; 62:846-856
2017	Hogan, R.E., et al., Bioavailability and Safety of Diazepam Intranasal Solution Compared to Oral and Rectal Diazepam in Healthy Volunteers, Epilepsia, 61:455-464 (Feb. 2020)
2018	Lindsay M. Higdon and Michael R. Sperling, A Review of a Diazepam Nasal Spray for the Treatment Of Acute Seizure Clusters and Prolonged Seizures, J Expert Review of Neurotherapeutics 2021; 21(11):1207-1212
2019	Bechgaard et al., Solubilization of Various Benzodiazepines for Intranasal Administration, a Pilot Study, Pharmaceutical Development and Technology 1997; 2(3):293-296
2020	Gizurarson, S., et al., Intranasal Administration of Diazepam Aiming at the Treatment of Acute Seizures: Clinical Trials in Healthy Volunteers, Biol. Pharm. Bull., 22(4):425-427 (Apr. 1999)
2021	Ivaturi, V.D., et al., Bioavailability and Tolerability of Intranasal Diazepam in Healthy Adult Volunteers, Epilepsy Res., 84:120-126 (2009)

Exhibit	Description of Exhibits
2022	Schrier, L., et al., Pharmacokinetics and Pharmacodynamics of a New Highly Concentrated Intranasal Midazolam Formulation for Conscious Sedation, Brit. J. Clin. Pharmacol., 83:721-731 (Apr. 2017)
2023	Penovich et al., Benzodiazepines for the Treatment of Seizure Clusters, CNS Drugs 2024; 38:125-140
2024	Kapoor et al., A Review of Intranasal Formulations for the Treatment of Seizure Emergencies, Journal of Controlled Release 2016; 237: 147-159
2025	Rabinowicz et al., Improvement of Intranasal Drug Delivery with Intravail® Alkylsaccharide Excipient as a Mucosal Absorption Enhancer Aiding in the Treatment of Conditions of the Central Nervous System, Drugs in R&D 2021; 21:361-369
2026	Acorda Therapeutics, Letter to Plumiaz Clinical Trial Participants, May 20, 2016
2027	U.S. Patent No. 6,193,985 (“Sonne”)
2028	NOT USED
2029	NOT USED
2030	Written joint research agreement, titled “Master Service Agreement” (7 pages), between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated April 1, 2007 [FILED UNDER SEAL]
2031	Asset Purchase Agreement between Hale BioPharma Ventures, LLC and Questcor Pharmaceuticals, Inc., dated June 27, 2008 [FILED UNDER SEAL]
2032	H.R. Rep. No. 108-425 (2004)
2033	150 Cong. Rec. S7520-05 (2004)

Exhibit	Description of Exhibits
2034	Non-disclosure Agreement between Aegis Therapeutics, LLC and Questcor Pharmaceuticals, Inc., dated August 15, 2005 [FILED UNDER SEAL]
2035	Confidentiality Agreement between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated January 19, 2007 [FILED UNDER SEAL]
2036	Email between Questcor Pharmaceuticals, Inc. and Aegis Therapeutics, LLC, dated February 15, 2007 [FILED UNDER SEAL]
2037	Quote No. QCR 135 between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated March 28, 2007 [FILED UNDER SEAL]
2038	QSC-002 Project Email Thread between Aegis Therapeutics, LLC and Questcor Pharmaceuticals, Inc., dated March 26, 2007
2039	Redline Comparison between U.S. Patent No. 11,793,786 and U.S. Patent No. 11,241,414
2040	QC and PSI Agreement between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated April 2, 2008 [FILED UNDER SEAL]
2041	Letter Agreement, with Term Sheet between Neurelis, Inc. and Aegis Therapeutics, LLC, dated August 28, 2007 [FILED UNDER SEAL]
2042	Supply Agreement Neurelis, Inc. and Aegis Therapeutics, LLC, dated May 22, 2008 [FILED UNDER SEAL]
2043	License Agreement Neurelis, Inc. and Aegis Therapeutics, LLC, dated May 22, 2008 [FILED UNDER SEAL]
2044	Transmittal Notice of Intravail from Aegis Therapeutics, dated October 2, 2008 [FILED UNDER SEAL]
2045	Declaration of Steven Cartt [FILED UNDER SEAL]

Exhibit	Description of Exhibits
2046	Declaration of Dr. Mark Mitchnick [FILED UNDER SEAL]
2047	Declaration of David Hale
2048	Redline Comparison between U.S. Patent Application No. 15/955,397 and U.S. Patent Application No. 17/228,514
2049	Marc Brown Curriculum Vitae
2050	Joint Claim Construction Brief, Neurelis, Inc. v. Padagis LLC et al., 1:24-cv-00562, D.I. 87 (D. Del. August 15, 2025) (“Joint CC Brief”)
2051	Andrew Streitwieser, Introduction to Organic Chemistry (4th ed. 1992) (“Streitwieser”)
2052	David W. Oxtoby et al., Principles of Modern Chemistry (4th ed. 1999) (“Oxtoby”)
2053	European Pharmacopoeia 6.0, Vol 2 (6th ed. 2007) (“PhEur 6.0”)
2054	Panayiotis P. Constantinides et al., Advances in the Use of Tocols as Drug Delivery Vehicles, 23 Pharm Res. 243 (2006) (“Constantinides-2006”)
2055	Rowe, Sheskey, & Owen, Handbook of Pharmaceutical Excipients, (6th ed. 2009) (“Rowe-2009”)
2056	Afaf Kamal-Eldin, Effect of Fatty Acids and Tocopherols on the Oxidative Stability of Vegetable Oils, 108 Eur. J. of Lipid Sci. & Tech. 1051 (2006) (“Kamal-Eldin-2006”)
2057	Branka Rozman & Mirjana Gašperlin, Stability of Vitamins C and E in Topical Microemulsions for Combined Antioxidant Therapy, 14 Drug Delivery 235 (2008) (“Rozman-2007”)

Exhibit	Description of Exhibits
2058	Afaf Kamai-Eldin & Lars-Ake Appelqvist, The Chemistry and Antioxidant Properties of Tocopherols and Tocotrienols, 31 Lipids 671 (1996) (“Kamai-Eldin-1996”)
2059	March 2009 FDA Inactive Ingredient Database
2060	Redline Comparison between U.S. Patent Application No. 12/413/439 and U.S. Patent Application No. 15/955,397
2061	David Ward, Optimizing Nasal Products for Systemic Delivery, 106 ONdrugDelivery 56 (2020) (“Ward-2020”)
2062	C. Holvoet et al., Inclusion Complexation of Diazepam with Different Cyclodextrins in Formulations for Parenteral Use, 60 Pharmazie 598 (2005) (“Holvoet-2005”)
2063	Sila-On et al., Influence of Incorporation Methods on Partitioning Behavior of Lipophilic Drugs into Various Phases of a Parenteral Lipid Emulsion, 9 PharmSciTech 684 (2008) (“Sila-On-2008”)
2064	D. J. Van Drooge et al., Incorporation of Lipophilic Drugs in Sugar Glasses by Lyophilization using a Mixture of Water and Tertiary Butyl Alcohol as Solvent, 93 J. of Pharm. Sci. 713 (2004) (“Van Drooge-2004”)
2065	L. M. A. Monzon & L. M. Yudi, Voltammetric Analysis of Lipophilicity of Benzodiazepine Derivatives at the Water 1,2-dichloroethan Interface, 495 J. of Electroanalytical Chem. 146 (2001) (“Monzon-2001”)
2066	M. Molero-Monfort et al., Retention-activity Relationship Studies of Benzodiazepines by Micellar Liquid Chromatography, 13 Biomed. Chromatography 394 (1999) (“Molero-Monfort-1999”)
2067	M. Molero-Monfort et al., Micellar Liquid Chromatography for Prediction of Drug Transport, 870 J. of Chromatography 1 (2000) (“Molero-Monfort-2000”)

Exhibit	Description of Exhibits
2068	Neurelis Patent Family Tree
2069	Declaration of Mareen Donovan, Ph.D. in Support of Defendants' Responsive Claim Construction Brief, Neurelis, Inc. v. Padagis LLC et al., 1:24-cv-562, D.I. 88-28 (D. Del. August 22, 2025) ("Donovan-CC Decl.")
2070	Certified transcription of December 10-11, 2025, Volume I and II Deposition of Maureen Donovan, Ph.D. in Padagis US LLC vs. Neurelis, Inc., IPR2025-00464, IPR2025-00465, IPR2025-00466 ("Donovan Transcript")
2071	What is Log P and How Does It Predict Chemical Behavior?, Biology Insights, (August 16, 2025), https://biologyinsights.com/what-is-log-p-and-how-does-it-predict-chemical-behavior/ ("Log P")
2072	Declaration of Dr. Marc Brown regarding U.S. Patent No. 8,895,546
2073	NOT USED
2074	NOT USED
2075	Statutory Disclaimer for Claims 1-16 and 18-21 of '546 Patent
2076	Patent Owner Response, dated November 5, 2019 in Aquestive Therapeutics, Inc. v. Neurelis, Inc., IPR2019-00451
2077	U.S. Patent No. 12,268,664 (the "'664 Patent")
2078	Certificate of Correction for U.S. Patent No. 12,268,664
2079	Defendants' Notice of Non-Party Subpoenas, Neurelis, Inc. v. Padagis LLC et al., 1:24-cv-562, D.I. 63 (D. Del. May 13, 2025)
2080	Non-Party Inventors' Responses to Subpoenas (D. Del. May 27, 2025)

Exhibit	Description of Exhibits
2081	Email from Board (Nov. 18, 2025) authorizing moving Due Date 1 (highlighting added)
2082	IPR2025-00464, Paper 43, Petitioner's Reply to Patent Owner's Response (Mar. 31, 2026), with highlighting added to show portions that Patent Owner seeks to strike
2083	IPR2025-00464, Exhibit 1078, Reply Declaration of Maureen Donovan, Ph.D. (Mar. 31, 2026), with highlighting added to show portions that Patent Owner seeks to strike

Neurelis (“PO”) submits this Sur-Reply to Petitioner’s Reply (Paper 43, “Reply”), challenging claims 17 and 22 of U.S. Patent No. 8,895,546 (EX1001, “’546 Patent”).

The concerns expressed by Neurelis in its Patent Owner Response (Paper 28, “POR”) remain unaddressed. Petitioner continues to follow the “inventor’s own path” in its obviousness arguments, but that “path itself never leads to a conclusion of obviousness; that is hindsight.” *Otsuka Pharm. Co., Ltd. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012). Petitioner starts with Gwozdz-PCT (EX1009) and modifies it with Meezan (EX1010), each of which shares inventors with the ’546 Patent. What matters is not the path forged by the inventors, but instead “the path that the person of ordinary skill in the art would have followed, as evidenced by the pertinent prior art.” *Millenium Pharms., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017) (quoting *Otsuka*, 678 F.3d at 1296). Petitioner’s Reply does not address either *Otsuka* or *Mellenium*, and Petitioner does not deny that it is simply seeking to retrace the inventors’ path. When reviewing the cited prior art from the perspective of a POSITA, there is no motivation to combine to achieve the claimed invention, absent Petitioner’s hindsight perspective of the inventor’s own work.

I. COLLATERAL ESTOPPEL DOES NOT APPLY

As is undisputed, the ’546 Patent was never actually litigated during IPR2019-00451. Only the ’876 Patent was litigated. Petitioner seeks to collapse the two

patents into one another through collateral estoppel, but “separate patents describe separate and distinct inventions, and it cannot be presumed that related patents rise and fall together.” *Comair Rotron, Inc. v. Nippon Densan Corp.*, 49 F.3d 1535, 1539 (Fed. Cir. 1995).

Petitioner’s attempts to shoehorn IPR2019-00451 into the ’546 Patent also fail because Claims 17 and 22 of the ’546 Patent include a limitation requiring dodecyl maltoside, which was not litigated in evaluating motivation to combine concerning the ’876 Patent, and the Gwozdz-PCT priority issues were not litigated and are subject to an intervening change in law.

A. ISSUES MATERIALLY DIFFER

Collateral estoppel does not apply when claims are “materially different” from those previously litigated. *ParkerVision, Inc. v. Qualcomm Inc.*, 116 F.4th 1345, 1356 (Fed. Cir. 2024); *MaxLinear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1377-78 (Fed. Cir. 2018) (remanding for failure to analyze dependent claims).

Every ’546 Patent claim requires “dodecyl maltoside.” In contrast, the sole independent claim of the ’876 Patent (claim 1) recites a broad genus, “alkyl glycoside,” and only certain dependent claims (claims 26-28, 30-33) recite “dodecyl maltoside.” The broader category of alkyl glycosides encompasses countless species of structurally distinct molecules varying in characteristics such as chain length (i.e., how many carbons, with “dodecyl” having 12 and “alkyl” having any number).

EX2072 ¶¶80, 189. These structural differences are not academic; they alter functional and biologic properties. EX2070 at 22:10-23:22, 25:13-25:24. This distinction matters because, as discussed below, the IPR2019-00451 panel treated the “alkyl glycoside” independent claims as representative, and swept in the remaining claims without further analysis.

Petitioner’s cited cases are inapposite. In *Ohio Willow Wood*, patent owner had “not provided any explanation regarding *how*” the difference in claim scope affects the invalidity analysis. *Ohio Willow Wood Co. v. Alps South, LLC*, 735 F.3d 1333, 1343 (Fed. Cir. 2013). In *Soverain*, the adjudicated claims recited a “network,” while the unadjudicated claim recited, “the network is an Internet.” “Routine incorporation of Internet technology ... does not change the invalidity analysis.” *Soverain Software LLC v. Victoria’s Secret Direct Brand Mgmt., LLC*, 778 F.3d 1311, 1319-1320 (Fed. Cir. 2015). Here, differences in claim language materially affect patentability.

“Obviousness concerns whether a skilled artisan not only could have made but would have been motivated to make the combinations or modifications of prior art *to arrive at the claimed invention*.” *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) (cleaned up). Meezan discloses a number of different alkyl glycosides, many of which perform better than “dodecyl maltoside.” As discussed further below, a POSITA would not have been motivated to combine Gwozd-PCT

with Meezan to arrive at the claimed invention. “[A] difference in the claims that would alter a POSITA’s motivation to combine prior art references would be material to the invalidity analysis.” *TQ Delta, LLC v. 2Wire, Inc.*, 2021 WL 2671296 at *6 (D. Del. June 29, 2021). Petitioner disregards this case.

B. ISSUES WERE NOT ACTUALLY LITIGATED

Collateral estoppel also fails because it applies only to issues “actually litigated in the first action.” *Google v. Hammond Development Int’l, Inc.*, 54 F.4th 1377, 1381 (Fed. Cir. 2022). Collateral estoppel does not apply to issues that merely “*could have been raised* in the prior litigation.” *Purdue Pharma L.P. v. Iancu*, 767 F. App’x 918, 922 (Fed. Cir. 2019) (cleaned up) (original emphasis). Failure to contest an issue, or even stipulating to it, does not create collateral estoppel. *Id.*

1. Non-Obviousness over Gwozdz-PCT and Meezan

Petitioner suggests that because several dependent claims of the ’876 Patent recited “dodecyl maltoside,” the ’546 Patent should be treated as having been actually litigated. Reply at 2-6. Petitioner is wrong.

In IPR2019-00451, patent owner did not contest whether the prior art disclosed any claim limitations, including “dodecyl maltoside.” EX2076 at 28-29; EX1072 ¶¶76-77 (expert presenting argument for motivation “to include alkyl glycosides,” but not addressing dodecyl maltoside); EX1040 at 27 (final written decision stating “Patent Owner does not present separate arguments for any of the

dependent claims.”). Nor did patent owner argue on appeal whether the prior art disclosed any of the claim limitations, or substantive non-obviousness of “dodecyl maltoside.” EX1081 (appellant’s opening brief) at 40-51. The only argument patent owner presented regarding “dodecyl maltoside” concerned priority date of the ’876 Patent, not non-obviousness. *See id.* at 1 (Question 2), 40 (non-obviousness section) 55-56 (remedy). The only non-obviousness arguments made concerning “dodecyl maltoside” was that Gwozdz-PCT did not qualify as prior art. *Id.* at 40.

2. Priority of Gwozdz-PCT

In IPR2019-00451, “Patent Owner [did] not contest that Gwozdz[-PCT] is entitled to this filing date” of Gwozdz-Provisional. EX1040 at 14. As this Panel explained:

On the present record, we agree with Patent Owner that collateral estoppel does not bar Patent Owner from challenging Gwozdz’s prior-art status in this case. Patent Owner’s apparent concession that Gwozdz was prior art during the 451 IPR does not equate to the issue being actually litigated. ... Failure to contest an issue – or even stipulating to an issue – does not comprise litigating that issue for collateral estoppel purposes. *See Purdue Pharma L.P. v. Iancu*, 767 F. App’x. 918, 922 (Fed. Cir. 2019).

Paper 13 at 15. Petitioner does not address this argument, nor recent authority on priority-date analysis. Paper 28 (“POR”) at 53-54; *In re Riggs*, 131 F.4th 1377, 1384 (Fed. Cir. 2025).

II. PETITIONER CONFLATES §103(c) PROVISIONS

Petitioner argues, “[w]ithout co-ownership, the safe harbor of Section 103(c)(2) cannot apply.” Reply at 12. While 35 U.S.C. §103(c)(1) (pre-AIA) requires actual co-ownership, §103(c)(2) does not. If the §103(c)(2) sub-provisions are met, subject matter developed by another is “deemed to have been owned by the same person or subject to an obligation of assignment to the same person.” Nevertheless, the §103(c)(2) argument is moot in this proceeding (subject to review and appeal) after the Board denied PO’s motion for leave to amend the specification. Papers 36, 39. Petitioner agrees that the argument under “35 U.S.C. §103(c)(2) is now moot” in this proceeding in view of these rulings. Reply at 1.

III. GWOZDZ-PCT IS NOT PRIOR ART

For Gwozdz-PCT to achieve a §102(e) (pre-AIA) prior art date to the 61/040,281 provisional, “the cited content” relied on to support the unpatentability analysis must also be “adequately supported by the written description of the provisional application.” *Riggs*, 131 F.4th at 1384-85.

In the Petition, Petitioner argued that “a motivation existed to combine” Gwozdz-PTC with Meezan, because “Gwozdz[-PCT] teaches that the pharmaceutical solutions ... may further incorporate additional pharmaceutically acceptable additives, including ... ‘penetration enhancers’ ... to improve the efficacy.” Pet. at 26-27 (citing EX1009, 10:12-16); *see* Pet. at 30, 44; EX2070

(Donovan Tr.) at 78:22-79:6. Elsewhere in the Petition, Petitioner asserts motivation to combine based on increasing “penetration and absorption.” Pet. at 31. The “penetration enhancer” embodiment was so important to Petitioner’s motivation to combine theory that Petitioner argued that collateral estoppel should apply specifically to the issue of whether “a person of ordinary skill in the art would have had reason to add alkyl glycoside as a penetration enhancer, as disclosed in Meezan.” Pet. at 9.

In response, PO explained how the “penetration enhancer” language was omitted by Gwozdz-Provisional, such that it is not prior art and not available to supply motivation to combine. POR at 16-17. Petitioner does not respond to the lack of disclosure of “penetration enhancer” in Gwozdz-Provisional or attempt to establish its availability as prior art. Rather, Petitioner sidesteps its own Petition, now asserting that “Petitioner’s obviousness showing does not depend on that phrase [‘penetration enhancer’] in any event.”¹ Reply at 1-2. Petitioner then shifts to a new theory in Reply concerning “wetting agents,” but as discussed below, this too does not support obviousness.

¹ This tactic is reminiscent of Obi-Wan Kenobi’s classic line, “These aren’t the drones you’re looking for.”

IV. THE CHALLENGED CLAIMS ARE NOT OBVIOUS

The combination of Gwozdz-PCT/Meezan does not render obvious any claims. First, the combination does not disclose all claim limitations. Second, Petitioner fails to present a compelling reason why a POSITA would combine the references, while ignoring the numerous reasons dissuading from such a combination. Petitioner's obviousness rationales are rife with hindsight.

A. FAILURE TO DISCLOSE OR SUGGEST ALL CLAIM LIMITATIONS

“[P]etitioner has the burden from the onset to show with particularity with the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016). “[A]n entirely new theory of prima facie obviousness” cannot be raised in reply, even if it “is responsive to the patent owner’s response.” *Corephotonics, Ltd. v. Apple Inc.*, 84 F.4th 990, 1008 (Fed. Cir. 2023); *see* Paper 48. It is not permissible for a reply to include “previously unidentified portions of a prior-art reference to make a meaningfully distinct contention” and cite “several new non-patent literature references” to support obviousness opinions. *Apple Inc. v. Andrea Elecs. Corp.*, 949 F.3d 697, 706 (Fed. Cir. 2020). Here, Petitioner introduces new evidence and theories.

Petitioner failed to explain how the prior art meets the “consisting of” limitation when the Petition relied on aqueous embodiments of the prior art. POR

at 26-28. Even after abandoning its previous claim-construction positions and relying on new embodiments, Petitioner still cannot demonstrate this limitation.

a. Petitioner's Improper Claim Construction Tactics

The challenged claims require a formulation “consisting of” various elements, none of which is water. In district court, Petitioner narrowly construed “consisting of” to mean either the claims must exclude all water or the claims are indefinite. EX2050 at 27, 46, 53-57. Dr. Donovan prepared a declaration espousing this very position. EX2069 ¶¶26, 33, 50, 53, 57.

The Petition did not identify these constructions. Every prior art embodiment the Petition cites explicitly contains water. POR at 25-28. For example, the “penetration enhancer” and “wetting” embodiments are within the “other pharmaceutically acceptable additives” disclosure in Gwozdz-PCT, which Petitioner relies on as supplying motivation to combine. EX1009 at 10:3-16. This embodiment is expressly aqueous, in “saline solution or water.” EX1009 at 10:8. Petitioner sought “broader constructions at the Board to support a patentability challenge while seeking narrower constructions in litigation to avoid infringement liability.” *Revvo Techs., Inc. v. Cerebrum Sensor Techs., Inc.*, IPR2025-00632, Paper 20 at 4 (P.T.A.B. Nov. 3, 2025) (precedential).

Faced with this inconsistency and failure to address the scope of “consisting of” in prior art, Petitioner changes horses. The day before filing Petitioner's Reply,

Petitioner unilaterally filed a “stipulation” in district court to withdraw its claim-construction position. EX1083. Dr. Donovan also asks the Board to ignore her district court declaration. EX1078 ¶¶15-16.

First, the rules do not permit parties to assert inconsistent claim constructions. Second, Petitioner now asserts new theories for how the prior art is non-aqueous (discussed below). Third, as Petitioner knows, at least one co-defendant has *not* offered such a stipulation and pursues the same argument based on “consisting of.” Such gamesmanship is not permitted.

Petitioner violated 37 C.F.R. §42.104(b)(3), which “requires *a petition* to identify ‘[h]ow the challenged claim is to be construed.’” *Tesla, Inc. v. Intellectual Ventures II LLC*, IPR2025-00340, Paper 18 at 2 n.1 (P.T.A.B. Nov. 5, 2025) (informative). Petitioner states that “[i]n the litigation, Petitioner agreed to adopt Patent Owner’s proposed construction” of “no construction necessary” (Reply at 7), but this “does not explain sufficiently why the different positions were warranted.” *Revvo*, IPR2025-00632, Paper 20 at 5 (rejecting excuse that petitioner “accepts Patent Owner’s proposed constructions”).

b. Petitioner Shifts to New Theories in Reply

Petitioner pivots to a new embodiment of Gwozdz-PCT as purportedly teaching non-aqueous intranasal solutions. Reply at 15, 22 (citing EX1009 at 11:17-18). This embodiment was not cited in the Petition and is improper in reply. *Ariosa*

Diagnostics v. Verinata Health, Inc., 805 F.3d 1359, 1367 (Fed. Cir. 2015) (“Not until ... Reply declaration did Ariosa identify specific embodiments ... that do not use restriction-enzyme digestible primers.”); *Corephotonics*, 84 F.4th at 1009 (reply is improper if it “‘point[s] to any new embodiments’ of a prior art reference not previously identified in the petition”). This new embodiment does not demonstrate obviousness.

c. No Motivation to Combine

The newly cited embodiment of Gwozdz-PCT states, “Formulations suitable for parenteral administration can be aqueous or non-aqueous *injection* solutions.” EX1009 at 11:17-19; Reply at 15, 22. An injection embodiment definitionally provides “absolute or 100% bioavailability.” EX2072 ¶109 (i.e., injections serve as the benchmark for bioavailability measurements). But according to the Petition, the motivation to combine Gwozdz-PCT and Meezan is for “improved bioavailability.” Petition at 30-32. If the new embodiment from Gwozdz-PCT is already 100% bioavailable (i.e., an injection), there would be no reason to modify Gwozdz-PCT with Meezan, as Gwozdz-PCT already provides 100% bioavailability.

The hindsight continues: every example in Meezan is directed to adding alkyl glycosides to aqueous solutions of peptides or proteins. EX2072 ¶139. Against the weight of disclosure, Petitioner cites the singular instance of the word “non-aqueous,” found in a boilerplate catch-all paragraph of Meezan. Reply at 24 (citing

EX1010 ¶[0074]). Petitioner is improperly “us[ing] hindsight reconstruction to pick and choose among isolated disclosures to deprecate the claimed invention.” *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1998); *Fulton*, 391 F.3d at 1200 (“whether there is something in the prior art as a whole to suggest the *desirability*, and thus the obviousness, in making the combination available”).

Petitioner relies on a different passage of Meezan for its disclosure of DDM. Reply at 25 (citing EX1010 ¶[0157]). But this passage discloses “ocular [eyedrops] administration of insulin” (a macromolecule), not intranasal administration of diazepam (small molecule).² EX1010 ¶[0157].

To reconstruct the challenged claims, requiring a non-aqueous intranasal solution of dodecyl maltoside and diazepam, Petitioner starts with an injection solution of benzodiazepines in Gwozdz (EX1009 at 11:17-26) that definitionally has 100% bioavailability. Petitioner modifies that solution by combining with an embodiment of Meezan directed to aqueous insulin eye drops, while simultaneously relying on a “non-aqueous” boilerplate statement. This is unbridled hindsight.

² The molecular weight of insulin is 5,800 Daltons, compared to 285 Daltons for diazepam. EX1077 at 214:12-17; EX2072 ¶169.

B. PETITIONER’S GENERIC MOTIVATIONS DO NOT ESTABLISH OBVIOUSNESS

Petitioner generically asserts that a “POSA in the field of pharmaceutical dosage form development is motivated to pursue better physicochemical properties, including solubility, stability, and bioavailability.” Reply at 17. This argument reduces to the truism that nothing is perfect, and any formulation can always be better. EX1077 at 129:2-16. But that is not the law. *ActiveVideo Networks, Inc. v. Verizon Commc’ns, Inc.*, 694 F.3d 1312, 1327-1328 (Fed. Cir. 2012) (generic testimony “fails to explain why a person of ordinary skill in the art would have combined elements from specific references *in the way the claimed invention does.*”); *Pers. Web Techs., LLC v. Apple, Inc.*, 848 F.3d 987, 992 (Fed. Cir. 2017) (rejecting rationale that a POSITA “once presented with the two references, would have understood that they *could* be combined”). None of Petitioner’s generic solubility, stability, and bioavailability theories pass muster.

1. Gwozdz-PCT Solves the Problem of Bioavailability

As discussed above, the aqueous embodiments cited from Gwozdz-PCT (injectables) are already 100% bioavailable. Thus, bioavailability cannot provide any motivation. EX1009 at 7:5-8 (Gwozdz-PCT already “provid[es] increased bioavailability of the therapeutic agent”).

2. Gwozdz-PCT Solves the Problem of Solubility

Petitioner relies on the patent itself to frame the problem of solubility. POR at 28. Petitioner responds with the non-sequitur that PO denies the existence of solubility problems in prior art other than Gwozdz-PCT. Reply at 17. The issue is that Petitioner employs “hindsight reconstruction by using the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.” *In re NTP, Inc.*, 654 F.3d 1279, 1299 (Fed. Cir. 2011) (cleaned up).

Petitioner fails to respond to the fact that Gwozdz-PCT already solved the problem. Reply at 17. Absent evidence, Petitioner speculates that a “POSA would have nonetheless been motivated to look to additional strategies to ... increase absorption and bioavailability.” Reply at 17-18. But Petitioner identifies no shortcomings in Gwozdz-PCT or need for improvement. Petitioner has not demonstrated that its “[f]ormulation of the problem was derived directly from the prior art, rather than from the challenged claims.” *Purdue Pharma L.P. v. Depomed, Inc.*, 643 F. App’x 960, 966 (Fed. Cir. 2010).

3. The Combination Does Not Improve Stability

Petitioner does not dispute that its own exhibits demonstrate negative interactions between benzyl alcohol, ethanol, and *n*-dodecyl- β -D-maltoside. Instead, Petitioner contends without any evidence (other than Dr. Donovan’s

unsupported musings) that these interactions “would not impact a POSA[.]” Reply at 18. The ’546 claims are not limited to “a one-time use product,” as Petitioner contends, which might otherwise minimize these concerns. *Medtronic, Inc. v. Teleflex Innovations S.a.r.l.*, 69 F.4th 1341, 1349 (Fed. Cir. 2023) (POSITA would consider whether “a proposed modification would interfere with a reference’s stated purpose”). Petitioner ignores this case. Nor does Petitioner acknowledge that ethanol was already a known penetration enhancer, to which a POSITA would not have been motivated to add a second one. POR at 34-35.

Tocopherols were known to be unstable. EX2070 at 283:18-284:13. Petitioner’s replies that “Gwozdz[-PCT] ... teach[es] formulations containing one or more tocopherols” and that other ingredients may be added. Reply at 19. But given the stability issues of tocopherols, a POSITA would have been dissuaded from modifying a working formulation absent a compelling reason. EX2072 ¶¶82-88, 173-177 (citing EX2053-EX2059). Petitioner’s reference to tocopherols with “additional pharmaceutically acceptable additives” appears in the embodiment on injection applications, not nasal administrations, and Meezan fails to teach any application to tocopherol-based solutions. POR at 40-41.

At bottom, nothing would have motivated a POSITA to improve Gwozdz-PCT, let alone with the disclosures of Meezan. Petitioner’s asserted motivation to

combine reduces to: any pharmaceutical solution can always be made better. Such a generalized desire to improve prior-art formulations does not establish a reason to combine prior-art elements “in the way the claimed new invention does.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007); *Virtek Vision Int’l ULC v. Assembly Guidance Sys., Inc.*, 97 F.4th 882, 887 (Fed. Cir. 2024) (“mere fact that these possible arrangements existed in the prior art does not provide a reason that a skilled artisan would have” made the combination).

Petitioner’s cited cases also do not stand for the proposition that such generalized goals of improvement could supplant the required motivation to combine analysis. In *Pfizer*, the patent challenger presented an “obvious to try” case, but it was supported by “numerous other publications [that] clearly directed the skilled artisan to” the combination. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1366 (Fed. Cir. 2007). The “prior art provided not only the means of creating [the combination] but also predicted the results, which [patentee] merely had to verify through routine testing.” *Id.* at 1367. The Federal Circuit found obviousness not based on generalizations of formulation improvement, but instead “on the particularized facts of this case.” *Id.* In contrast, Petitioner does not present “particularized facts” but instead generalizes that a POSITA “is motivated to pursue better physiochemical properties, including solubility, stability, and bioavailability.” Reply at 17. This is hindsight, not motivation to combine.

C. PETITIONER’S RELIANCE ON “OTHER PHARMACEUTICALLY ACCEPTABLE ADDITIVES” AND “WETTING AGENTS”

The “penetration enhancer” embodiment is not prior art because it does not appear in Gwozdz-Provisional (EX1064). POR at 16-17. Petitioner does not dispute this. Reply at 20-21. Instead, Petitioner switches to Gwozdz’s “wetting ... materials” as an alleged motivation. Reply at 21; EX1009 at 10:9-16. This is a new theory, impermissible in reply.

Also, the “wetting ... materials” disclosure, like “other pharmaceutically acceptable additives,” appears in the embodiment on injection application, but not in the embodiment for “nasal applications.” EX1009 at 9:19-10:2, 10:3-16. The route of administration is an important factor in drug delivery, which Petitioner ignores. EX1077 at 140:19-142:3. Petitioner also ignores the purpose of a “wetting” agent, which “modifies interfacial tension of water” (i.e., aqueous). EX1010 ¶[0053]. Petitioner relies on *aqueous* injections as its motivation to combine to arrive at *non-aqueous* intranasal applications. This is another example of improper hindsight reconstruction. *Henny Penny*, 938 F.3d at 1332 (“[P]rior art must be considered for all its teachings, not selectively”).

D. MEEZAN IS DIRECTED TO MACROMOLECULES AND DOES NOT ADDRESS COMPATIBILITY WITH TOCOPHEROL SOLUTIONS

Petitioner asserts that a single disclosure of “small organic molecules” would teach a POSITA that Meezan could be applied to small molecules. Reply at 23-24.

Not so. A POSITA must “read the whole ... document to understand what [Meezan] mean[s] by small organic drug molecules.” EX1077, 154:6-8; POR at 38-40; *In re Fine*, 837 F.2d at 1075 (do not “pick and choose among isolated disclosures in the prior art to deprecate the claimed invention”). Petitioner does not identify any examples of small molecule applications in Meezan.

Petitioner does not respond to why a POSITA would even consider Meezan for small molecules, nor to the cases that PO cites regarding no motivation to combine when there are redundant effects. POR at 39-40.

Petitioner also claims that Meezan’s compounds may be used in aqueous or non-aqueous solutions. Reply at 24 (citing EX1010 ¶[074]). As stated and unrefuted by Petitioner, all of Meezan’s examples combine a disclosed compound in aqueous solutions of peptide or proteins (i.e., macromolecules). POR at 40-41. Petitioner is also still silent on the incompatibility of the Meezan compounds with tocopherol-containing solutions. POR at 41 (citing EX2070 at 149:7-150:7; EX2072 ¶[172]). Petitioner does not and cannot reconcile any disclosure of tocopherol-containing solutions like those of Gwozdz-PCT with that of Meezan. POR at 41.

E. NO MOTIVATION TOWARD DODECYL MALTOSE

Petitioner cites a single example, Meezan ¶[0157], which compares dodecyl maltoside (DDM), tridecyl maltoside, and tetradecyl maltoside (TDM) as “absorption enhancers for ocular administration of insulin” through ocular routes

(eyedrops). Reply at 25. The same paragraph describes TDM as having “the greatest effect,” but Petitioner ignores this and focuses on DDM (which is not the claimed compound). Reply at 25; EX1010 ¶[0157].

The *Fulton* case cited by Petitioner is inapposite. *Fulton* suggests that the “desirability of a particular combination need not be supported” by a preferred combination in the prior art. *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004). But in *Fulton* there were no other prior art findings that taught away from the “less desirable” combination. Meezan expresses a distinct preference for TDM. And in *Uber*, the Federal Circuit found obviousness because there were only two options: plot at the terminal (client) or at the server. *Uber Techs., Inc. v. X One, Inc.*, 957 F.3d 1334, 1340 (Fed. Cir. 2020). Choosing between options was simply a “design choice between the two.” *Id.* In pharmaceutical formulations such as these, Petitioner has not presented any evidence that choosing between TDM and DDM was simply a design choice, particularly when Meezan would lead a POSITA to choose TDM as preferred.

Petitioner ignores the full scope of Meezan and reviews Table I in a vacuum. A POSITA would look at all the Examples disclosed in Meezan and see that there is a quantifiable advantage of TDM over DDM. EX2072 ¶¶184-187. In Table III, decyl maltoside, dodecyl sucrose, and tridecyl maltoside all outperformed DDM at the same 0.5% concentration for decreasing the amount of blood glucose via

eyedrops (not intranasal) in rats. EX2072 ¶186. Table II shows that that 0.125% TDM eye drops were more effective than DDM. EX2072 ¶184. In short, nothing in Meezan suggests the desirability of using dodecyl maltoside in intranasal applications (as compared to TDM); nor does anything disclose or even suggest the use of the linear species, as opposed to “highly branched.”

V. CONCLUSION

Petitioner has failed to meet its burden of proving unpatentability of any '546 Patent claims.

Dated: May 12, 2026

/David J. Tobin/

David J. Tobin

(Reg. No. 60,776)

MCDERMOTT WILL & SCHULTE LLP

2801 North Harwood Street, Suite 2600

Dallas, TX 75201

Tel: (214) 210-2793

dtobin@mcdermottlaw.com

Counsel for Patent Owner

CERTIFICATION OF WORD COUNT

The undersigned hereby certifies that the portions of the above-captioned PATENT OWNER'S SUR-REPLY, contain 4,168 words, in compliance with the 5,600 word limit set forth in 37 C.F.R. § 42.24(c)(4). This word count was prepared using Microsoft Word 365 V.2503.

Dated: May 12, 2026

/David J. Tobin/

David J. Tobin

(Reg. No. 60,776)

MCDERMOTT WILL & SCHULTE LLP

2801 North Harwood Street, Suite 2600

Dallas, TX 75201

Tel: (214) 210-2793

dtobin@mcdermottlaw.com

Counsel for Patent Owner

CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing PATENT OWNER'S SUR-REPLY was served on counsel of record for the Petitioner by filing this document through PTAB P-TACTS and by sending the same via electronic mail to the following addresses:

James P. Murphy
Reg. No. 55,474
Polsinelli PC
1000 Louisiana Street
Suite 6400
Houston, Texas 77002
Tel: (713) 374-1600
jpmurphy@polsinelli.com

Corey Casey
Reg. No. 66,950
Polsinelli PC
900 West 48th Place
Suite 900
Kansas City, Missouri 64112
Tel: (816) 572-4439
ccasey@polsinelli.com

Mark Deming
Reg. No. 69,263
Polsinelli PC
150 N. Riverside Plaza Suite 300
Chicago, IL 60606
mdeming@polsinelli.com

Chad A. Landon
Provisionally Recognized Pro Hac Vice
Polsinelli PC
1401 I St. NW Suite 800
Washington, DC 20005
clandmon@polsinelli.com

Dated: May 12, 2026

/David J. Tobin/
David J. Tobin
(Reg. No. 60,776)
MCDERMOTT WILL & SCHULTE LLP
2801 North Harwood Street, Suite 2600
Dallas, TX 75201
Tel: (214) 210-2793
dtobin@mcdermottlaw.com

Counsel for Patent Owner