

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEURODERM LTD.,
Petitioner,

v.

ABBVIE INC.,
Patent Owner.

PGR2022-00040
Patent 11,091,507 B2

Before TINA E. HULSE, DEVON ZASTROW NEWMAN, and
CYNTHIA M. HARDMAN, *Administrative Patent Judges*.

HARDMAN, *Administrative Patent Judge*.

DECISION
Granting Institution of Post-Grant Review
35 U.S.C. § 324

I. INTRODUCTION

Petitioner NeuroDerm Ltd. requests post-grant review of claims 1–17 of U.S. Patent No. 11,091,507 B2 (“the ’507 patent,” Ex. 1001). Paper 2 (“Pet.”). Patent Owner AbbVie Inc. filed a Preliminary Response. Paper 6 (“Prelim. Resp.”). With our authorization, Petitioner filed a Preliminary Reply and Patent Owner filed a Preliminary Sur-reply. Paper 7 (“Reply”); Paper 8 (“Sur-reply”).

Considering the arguments and evidence presented, we institute a post-grant review because we determine that the Petition demonstrates “that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable.” 35 U.S.C. § 324(a).

The following preliminary findings of fact and conclusions of law are made solely to determine whether to institute review. Any final decision will be based on the full trial record.

A. Real Parties in Interest

Petitioner identifies itself and Mitsubishi Tanabe Pharma Corporation as the real parties in interest. Pet. 108.

Patent Owner identifies itself as the real party in interest. Paper 5 (Patent Owner Mandatory Notices), 1.

B. Related Matters

Patent Owner identifies pending U.S. Patent Application No. 17/378,321. Paper 5, 1. The parties do not identify any other related matters. *See id.*; Pet. 108.

C. The '507 Patent (Ex. 1001)

The '507 patent, titled “Methods of Treating Parkinson’s Disease,” “relates to (a) carbidopa prodrugs, (b) L-dopa¹ prodrugs, (c) pharmaceutical combinations and compositions comprising a carbidopa prodrug and/or an L-dopa prodrug, and (d) methods of treating Parkinson’s disease and associated conditions comprising administering a carbidopa prodrug and an L-dopa prodrug to a subject with Parkinson’s disease.” Ex. 1001, code (54), 1:19–25.

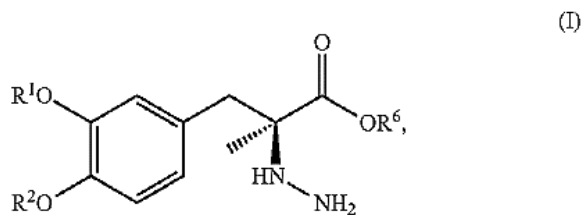
“Parkinson’s disease is a chronic and progressive neurodegenerative condition characterized by reduced levels in the brain of the neurotransmitter dopamine.” *Id.* at 1:29–31. “Administration of L-dopa . . . currently is the most effective therapy for treating a patient with Parkinson’s disease.” *Id.* at 1:32–34. However, due to premature peripheral metabolism of levodopa throughout the body, a relatively large levodopa dose is required, which can cause complications such as nausea. *Id.* at 1:55–63. “To overcome these problems, L-dopa generally is co-administered with a peripheral aromatic L-amino acid decarboxylase inhibitor such as carbidopa.” *Id.* at 1:58–2:9.

The Specification states that “[e]ven when L-dopa and carbidopa are co-administered, however, it is difficult to consistently maintain the desired dopamine levels in the brain due to the relatively short half-life of L-dopa in plasma.” *Id.* at 2:16–19. “One approach that has been effective in reducing variability of dopamine levels is the continuous intestinal delivery of an adjustable dose of an L-dopa/carbidopa gel known by its commercial name,

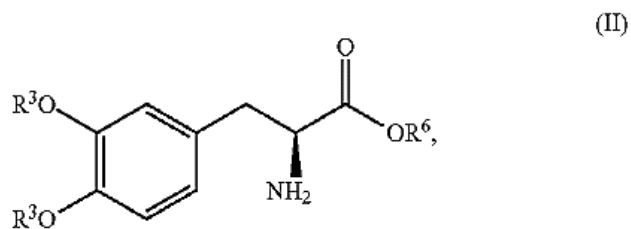
¹ “L-dopa” is shorthand for levodopa. *See* Pet. 10.

DuoDopa® in Europe and Duopa® in the United States.” *Id.* at 2:16–35. Achieving continuous intestinal delivery, however, requires a surgical procedure. *Id.* at 2:16–35. The Specification further states that “[a] major challenge to the development of less invasive or otherwise improved modes of administering L-dopa and carbidopa has been the solubility of those compounds.” *Id.* at 2:40–42. The ’507 patent thus states that “[s]table, more highly concentrated, and/or less viscous formulations comprising L-dopa and/or carbidopa (or compounds capable of in vivo bioconversion to L-dopa and/or carbidopa) are desirable.” *Id.* at 2:44–47.

The ’507 patent discloses compositions comprising “L-dopa and carbidopa prodrugs that convert to L-dopa and carbidopa in vivo[,] which allows for delivery by continuous administration methods including intragastric, intramuscular, intravenous, and subcutaneous administration.” *Id.* at 7:8–13. Regarding carbidopa prodrugs, the Specification provides compounds having the following Formula (I):



Id. at 3:3–20. In Formula (I) reproduced above, “R¹ and R² are each independently selected from the group consisting of hydrogen, –P(O)(OH)₂, and –R⁵–O–P(O)(OH)₂; R⁵ is a C₁–C₄-alkyl; R⁶ is hydrogen or a C₁–C₄-alkyl; and provided that at least one of R¹ and R² is –P(O)(OH)₂ or –R⁵–O–P(O)(OH)₂.” *Id.* Regarding levodopa prodrugs, the Specification provides compounds having the following Formula (II):



Id. at 3:21–39.² In Formula (II) reproduced above, “R³ and R⁴ are each independently selected from the group consisting of hydrogen, –P(O)(OH)₂, and –R⁵–O–P(O)(OH)₂; R⁵ is a C₁–C₄-alkyl; R⁶ is hydrogen or a C₁–C₄-alkyl; and provided that at least one of R³ and R⁴ is –P(O)(OH)₂ or –R⁵–O–P(O)(OH)₂.” *Id.*

The ’507 patent states that, in one aspect, the disclosure regards a method of treating Parkinson’s disease or an associated condition in a patient comprising administering to the patient a therapeutically effective amount of a pharmaceutical combination comprising a first compound corresponding in structure to Formula (I), or a pharmaceutically acceptable salt thereof, and a second compound corresponding in structure to Formula (II), or a pharmaceutically acceptable salt thereof.

Id. at 3:54–62. In Example 16, “[t]he in vivo conversion of the L-dopa phosphate prodrugs to L-dopa and the carbidopa phosphate prodrugs to carbidopa was evaluated in a rat pharmacokinetics study in which the prodrug was administered intravenously or subcutaneously to the rat.”

Id. at 82:34–41. In Example 19, “[t]he in vivo conversion of the carbidopa diphosphate to carbidopa was evaluated in a mini-pig pharmacokinetics study in which the prodrug was administered in aqueous solution subcutaneously to a group of three mini-pigs.” *Id.* at 85:54–61. Example 23

² The structural formula appears to contain a typographical error, in that the lower R³ should instead be R⁴. *See* Ex. 1001, 18:6–60; Pet. 23 n.84.

provides a study of local irritation and pain at the injection site in rabbits following “intravenous, paravenous, and subcutaneous bolus injection of LD/CD³ diphosphate at concentrations for 200/50 mg/mL.” *Id.* at 88:24–30.

D. Relevant Prosecution History

The ’507 patent issued from U.S. Patent Application Serial No. 16/866,400 (“the ’400 application”), filed on May 4, 2020. Ex. 1001, codes (21), (22). The ’507 patent claims earliest priority to Provisional Application No. 62/066,771, filed on October 21, 2014. *Id.* at code (60).

Upon filing, the ’400 application contained thirty claims. Ex. 1002, 172–79. Independent claim 1 recited a “pharmaceutical combination” comprising compounds of Formulas (I) and (II), and independent claims 13 and 18 respectively recited compounds of Formula (I) and Formula (II). *Id.* at 172, 176–77. Independent claim 30 recited “[a] compound selected from the group consisting of” compounds having structural formulas (a) to (u). *Id.* at 179–82.

In a Preliminary Amendment filed on May 4, 2020 (the same day the ’400 application was filed), the applicant canceled claims 1–30 and added claims 31–41. *Id.* at 2–4, 250, 535. Independent claim 31, the only independent claim, recited:

³ LD and CD are abbreviations for levodopa and carbidopa, respectively. *See, e.g.*, Ex. 1003 ¶ 69.

31. A method of delivering dopamine to a Parkinson's disease patient in a pharmacokinetically-consistent manner comprising, continuously administering an aqueous pharmaceutical formulation subcutaneously for a time period, the formulation comprising:

(a) a compound comprising levodopa,
(b) an L-amino acid decarboxylase inhibitor, and
(c) an aqueous carrier,
wherein the method achieves a steady state levodopa plasma level in the patient over the time period of about 1000 ng/ml to about 5000 ng/ml.

Id. at 3. Dependent claim 37 recited “wherein the L-amino acid decarboxylase inhibitor is carbidopa or a carbidopa prodrug.” *Id.*

In a Non-Final Office Action, the Examiner rejected the claims under 35 U.S.C. § 112(b) as failing to set forth the subject matter the inventors regarded as their invention. *Id.* at 547. Regarding the claim term “an L-amino acid decarboxylase inhibitor,” the Examiner stated that the specification “disclosed carbidopa, [0003] as the L-amino acid decarboxylase inhibitors and compounds of formula I, [0007] as being capable of in vivo conversion to carbidopa (prodrugs),” but “the claims are drawn to non-limiting L-amino acid decarboxylase inhibitors (claims 31-36, 38-41) and non-limiting carbidopa prodrugs (claim 37).” *Id.* In a subsequent interview, “the Examiner suggested limiting the inhibitors to applicant’s invention.” *Id.* at 623. The applicant amended claim 31 by replacing “an L-amino acid decarboxylase inhibitor” with “carbidopa, or a pharmaceutically acceptable salt thereof,” and canceled claim 37. *Id.* at 626, 679.

In a second Non-Final Office Action, the Examiner rejected the claims for non-statutory double patenting. *Id.* at 689–92. The applicant

submitted a terminal disclaimer and added “and wherein the time period is at least 8 hours” to claim 31. *Id.* at 699, 705. The Examiner issued a Notice of Allowance. *Id.* at 713.

The applicant then filed a Request for Continued Examination, in which it changed the application’s title from “CARBIDOPA PRODRUGS” to “METHODS OF TREATING PARKINSON’S DISEASE.” *Id.* at 725–28. The applicant also added dependent claims 39–47, directed to steady state levodopa blood levels. *Id.*

In a Non-Final Office Action, the Examiner rejected the claims under 35 U.S.C. § 112(b), finding the language added to claim 31 (“and wherein the time period is at least 8 hours”) to be ambiguous. *Id.* at 758–60. The Examiner suggested replacement language. *Id.* at 760. The Examiner also rejected the claims as obvious over Caraco Abstract LBA26⁴, asserting that “the claimed LD plasma level of 1000 to 5000 ng/ml was motivated by the suggestion by Caraco et al., that the level could be adjusted by adjusting the infusion rate” of ND0612, an “aqueous formulation of levodopa/carbidopa.” *Id.* at 763, 761.

To overcome the § 112(b) rejection, the applicant adopted the Examiner’s suggested claim amendments. *Id.* at 777. To overcome the obviousness rejection, the applicant amended claim 31 to recite “without co-administration of a catechol-O-methyl transferase inhibitor,” and argued that

⁴ Caraco et al., *ND0612, a Novel Formulation of Levodopa/Carbidopa for Continuous, Subcutaneous Administration, Achieves Steady-State Levodopa Plasma Concentrations in Parkinson’s Disease Patients*, Abstract LBA26 (Ex. 1002, 837, “Caraco LBA26 Abstract”).

Caraco Abstract LBA26 discloses co-administration of a catechol-O-methyl transferase (“COMT”) inhibitor. *Id.* at 774, 777–80.

The Examiner issued a Final Office Action, maintaining the obviousness rejection over Caraco Abstract LBA26. *Id.* at 815–22. The Examiner and applicant discussed the rejection at another interview, but “[n]o agreement was reached.” *Id.* at 828. The applicant filed a Request for Continued Examination, together with a Declaration from Dr. Martin M. Okun, M.D., Ph.D., which sought to distinguish Caraco Abstract LBA26. *Id.* at 829–69. The Examiner and applicant held another interview, and again “[n]o agreement was reached.” *Id.* at 1594. The interview summary states that “Applicant would consider amending the claims by adding dose (e.g. 5mg/ml, LD), [0165] and would consider addressing LD and prodrug in an affidavit.” *Id.*

The applicant next filed a Supplemental Amendment and Response, in which it amended claim 31 to recite “at least about 5 mg/mL of a compound comprising levodopa.” *Id.* at 1595–1600. The applicant also purported to summarize its interview with the Examiner, stating:

During the interview on June 4, 2021, the Examiner indicated that he would consider the claims to be allowable if the instant amendment to claim 31, specifying a concentration of the compound comprising levodopa, was made to the claim. The Examiner also suggested filing a declaration under 37 CFR § 1.132 in which one of skill in the art declared how the phrase “a compound comprising levodopa” would be construed.

Id. at 1599. The applicant also filed a second declaration by Dr. Okun, which stated:

As a person of skill in the art of organic chemistry, as a Ph.D. scientist, I interpret the phrase “a compound comprising levodopa” to include any molecule with a levodopa core moiety. This would include levodopa itself, as well as prodrugs, salts, and hydrates of levodopa.

Id. at 1601–02.

The Examiner allowed the claims, providing the following statement of reasons for allowance: “the 103 rejection is withdrawn due to the Oath and amendment filed 6/8/21.” *Id.* at 1613. The ’507 patent thereafter issued. *Id.* at 1656.

E. Illustrative Claim

Petitioner challenges all claims (1–17) of the ’507 patent. Claim 1, the only independent claim, reads:

1. A method of delivering dopamine to a Parkinson’s disease patient in a pharmacokinetically-consistent manner comprising, continuously subcutaneously administering an aqueous pharmaceutical formulation to the patient, the formulation comprising:

- (a) at least about 5 mg/mL of a compound comprising levodopa,
- (b) carbidopa, or a pharmaceutically acceptable salt thereof, and
- (c) an aqueous carrier,

wherein the method is sufficient to achieve a steady state levodopa plasma level of about 1000 ng/ml to about 5000 ng/ml in the patient for at least 8 hours without co-administration of a catechol-O-methyltransferase inhibitor.

Ex. 1001, 114:30–43.

Claims 2, 3, 9, 10, 12, and 13 relate to achieving a steady state levodopa plasma level in the patient for a certain number of hours. *Id.* at 114:44–49, 114:65–115:3, 115:7–12. Claim 4 recites that the steady state levodopa plasma level is achieved without an oral medication for

Parkinson's Disease. *Id.* at 114:50–52. Claims 5–8 and 11 recite specific steady state levodopa plasma levels. *Id.* at 114:53–64, 115:4–6. Claims 14–17 recite levodopa dosages. *Id.* at 115:13–24.

F. Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–17 are unpatentable on the following four grounds:

Claim(s) Challenged	35 U.S.C. §⁵	Reference(s)/Basis
1–17	112(a)	Written Description
1–17	112(a)	Enablement
1–5, 14–17	102(a)(1)	Yacoby-Zeevi ⁶
1–17	103	Yacoby-Zeevi, Nyholm ⁷

Pet. 4. Petitioner supports its arguments with declarations from Peter A. LeWitt, M.D. and Kenneth B. Sloan, Ph.D. Exs. 1003, 1004.

⁵ The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”), amended several provisions of 35 U.S.C., including §§ 102, 103, and 112. The earliest possible priority date for the challenged claims (*see supra* Section II.A) is after the effective date of the applicable AIA amendments. Accordingly, we refer to the AIA versions of these statutes.

⁶ Yacoby-Zeevi, O., et al., *Maintenance of Constant Steady State Therapeutic Plasma Concentrations of Levodopa Following Its Continuous Subcutaneous Administration with Carbidopa* (“Yacoby-Zeevi,” Ex. 1005).

⁷ Nyholm, D., et al., *Pharmacokinetics of Levodopa, Carbidopa, and 3-O-Methyldopa Following 16-hour Jejunal Infusion of Levodopa-Carbidopa Intestinal Gel in Advanced Parkinson's Disease Patients*, 15(2) THE AAPS JOURNAL 316–23, April 2013 (“Nyholm,” Ex. 1006).

II. ANALYSIS

A. *Post-Grant Review Eligibility*

The post-grant review provisions apply only to patents that contain a claim with an effective filing date on or after March 16, 2013. *See* Pub. L. No. 112-29, 125 Stat. 284 (2011), §§ 3(n)(1), 6(f)(2)(A).

The '507 patent issued from an application filed on May 4, 2020, and claims its earliest priority to a provisional application filed on October 21, 2014.⁸ Ex. 1001, codes (22), (60). Because the earliest possible priority date is after March 16, 2013, the '507 patent is eligible for post-grant review. Patent Owner does not dispute this eligibility.

B. *Level of Ordinary Skill in the Art*

We consider the grounds of unpatentability in view of the understanding of a person of ordinary skill in the art (sometimes referred to herein as a “skilled artisan”). *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). Factors pertinent to determining the appropriate level of skill in the art include:

(1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field. . . . The patent’s purpose can also be informative.

⁸ Petitioner contends that “[c]laims 1–17 are entitled to an effective filing date no earlier than October 21, 2015, the filing date of the first non-provisional application, and are not entitled to claim priority to Provisional App. No. 62/066,771, filed on October 21, 2014.” Pet. 6 n.8. Patent Owner does not take a position on the appropriate priority date, other than asserting it is prior to 2017. Prelim. Resp. 46 n.7. At this stage of the proceeding, we need not determine the specific priority date for the challenged claims.

Best Medical Int'l, Inc. v. Elekta Inc., 46 F.4th 1346, 1353 (Fed. Cir. 2022) (citations omitted).

The parties posit similar proposals for the appropriate skill level, but dispute whether a skilled artisan himself or herself would have needed to have experience treating Parkinson's disease, or whether it is sufficient that he or she have "access to" someone having such experience. Petitioner's proposal requires that the skilled artisan himself or herself have experience treating Parkinson's disease:

A hypothetical person of ordinary skill in the art of the '507 patent would have a medical degree, or a Ph.D. in a field related to the development of pharmaceuticals, or equivalent degree, and several years of experience in treating patients with Parkinson's disease and/or researching treatments for Parkinson's disease. The hypothetical person of ordinary skill would also have access to one or more persons holding an advanced degree in pharmacology, pharmacokinetics, pharmaceutics, pharmaceutical chemistry, medicinal chemistry, or a related field, with substantial experience in the analysis of pharmacokinetic data and/or pharmaceutical formulation development.

Pet. 45.

Patent Owner criticizes Petitioner's proposal for "prioritiz[ing] experience in the medical treatment of Parkinson's disease" while failing to require "experience in the analysis of pharmacokinetic data and/or pharmaceutical formulation development." Prelim. Resp. 19. Patent Owner thus proposes that a person of ordinary skill in the art would have:

(a) a Ph.D. in a field related to the development of pharmaceuticals (for example, pharmacology, pharmacokinetics, pharmaceutics, pharmaceutical chemistry, organic chemistry, biochemistry, molecular biology, medicinal chemistry, formulation development, or a related

field), or equivalent degree, and 2-4 years of experience in the analysis of pharmacokinetic data, pharmaceutical formulation development, and/or drug discovery or development, or would have a B.S. or M.S. degree in a field related to the development of pharmaceuticals, or equivalent degree, and 4-6 years of experience in the analysis of pharmacokinetic data, pharmaceutical formulation development, and/or drug discovery or development, and

(b) access to one or more team members having a medical degree or equivalent degree with experience in treating patients with Parkinson's disease.

Id. at 18.

Based on the current record, we determine that a person of ordinary skill in the art would have knowledge and skill in several scientific disciplines, including the treatment of Parkinson's disease, the analysis of pharmacokinetic data, and pharmaceutical formulation development. For example, the '507 patent "is directed to subcutaneous administration of an aqueous formulation to achieve continuous and consistent plasma levels of levodopa to treat Parkinson's disease." *Id.* at 19. The cited prior art indicates a close relationship between levodopa plasma levels and control of patient symptoms, and indicates that plasma levels are affected by dosage form and route of administration. Nyholm, for example, states:

The development of levodopa-associated motor complications may be related to the pulsatile dopaminergic stimulation characteristic of conventional oral levodopa regimens. Levodopa is rapidly metabolized and has a short plasma half-life of approximately 90 min (when administered with carbidopa), thus requiring frequent, repeated dosing. As levodopa is absorbed mainly in the proximal small intestine, gastric emptying plays an important role in determining plasma levodopa levels after intake of conventional oral formulations. Erratic gastric

emptying is common in PD and likely contributes to fluctuations in levodopa plasma levels and the unpredictable motor responses observed with orally dosed levodopa.

Ex. 1006, 1 (citations omitted). Accordingly, when considering the '507 patent's purpose, the type of problems encountered in the art, and prior art solutions to those problems, it is clear that with respect to levodopa/carbidopa treatments for Parkinson's Disease, the pharmaceutical formulation and its resulting pharmacokinetics and patient experience are intertwined, thus supporting a requirement that a person of ordinary skill in the art have knowledge or experience in each of these areas. *See, e.g., Indivior Inc. v. Dr. Reddy's Labs., S.A.*, 930 F.3d 1325, 1345 (Fed. Cir. 2019) (finding no clear error in district court's compromise measure of level of ordinary skill in the art as a team comprising different skill sets).

In view of the above considerations, we preliminarily find that a person of ordinary skill in the art would be a member of a team that includes person(s) with

(a) a Ph.D. in a field related to the development of pharmaceuticals (for example, pharmacology, pharmacokinetics, pharmaceutics, pharmaceutical chemistry, organic chemistry, biochemistry, molecular biology, medicinal chemistry, formulation development, or a related field), or equivalent degree, and 2–4 years of experience in the analysis of pharmacokinetic data, pharmaceutical formulation development, and/or drug discovery or development, or a B.S. or M.S. degree in a field related to the development of pharmaceuticals, or equivalent degree, and 4–6 years of experience in the analysis of

pharmacokinetic data, pharmaceutical formulation development, and/or drug discovery or development, and
(b) a medical degree or equivalent degree with experience in treating patients with Parkinson’s disease.

In subsequent briefing, should the parties propose any differences from the team approach articulated above, they should support their proposal and address the impact, if any, of the differences on the pertinent disputes in this proceeding. Any final determination on the level of ordinary skill in the art will be made on the full trial record.

Additionally, based on their statements of qualifications and curricula vitae, for purposes of this Decision we find Drs. LeWitt and Sloan qualified to provide technical opinions from the perspective of a person of ordinary skill in the art. Ex. 1003 ¶¶ 1–10, pp. 87–119 (Dr. LeWitt’s statement of qualifications and curriculum vitae); Ex. 1004 ¶¶ 1–11, pp. 45–71 (Dr. Sloan’s statement of qualifications).

C. Claim Construction

We interpret a claim “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b).” 37 C.F.R. § 42.100(b). Under this standard, we construe the claim “in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” *Id.*

For purposes of this Decision, we provide preliminary constructions for the terms “a compound comprising levodopa” and “patient.” At this stage we need not construe any additional terms. *See Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375 (Fed. Cir. 2019) (“The Board is required to construe ‘only those terms . . . that are in controversy, and only to the extent

necessary to resolve the controversy.”)(quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

Any final written decision entered in this case may include final claim constructions that differ from the preliminary understanding of the claims set forth below, or from any discussion of claim scope provided in our analysis below. Any final claim constructions will be based on the full trial record.

1. “a compound comprising levodopa”

Petitioner asserts that term “a compound comprising levodopa,” which appears in claim 1, “should be construed to include ‘any molecule with a levodopa core moiety, including levodopa itself, as well as prodrugs, salts, and hydrates of levodopa.’” Pet. 46. Petitioner argues that we should adopt this definition because during prosecution Patent Owner (as the applicant) “acted as its own lexicographer” via Dr. Okun’s declaration. *Id.* at 46–47 (citing Ex. 1002, 1599, 1601, 1613).

Patent Owner likewise asserts that Dr. Okun’s “express definition provided during prosecution should be adopted,” although Patent Owner cites only a truncated portion of the definition, namely, “any molecule with a levodopa core moiety.” Prelim. Resp. 17 (citing Ex. 1002, 1601).

We agree with the parties that the express definition provided during prosecution should be adopted. *See, e.g., Biotec Biologische Naturverpackungen GmbH v. Biocorp, Inc.*, 249 F.3d 1341, 1346–47 (Fed. Cir. 2001) (construing claims in accordance with definition provided in declarations submitted during prosecution). Accordingly, we preliminarily construe the term “a compound comprising levodopa” in accordance with the full definition Dr. Okun provided during prosecution, i.e., “any molecule

with a levodopa core moiety including levodopa itself, as well as prodrugs, salts, and hydrates of levodopa.”

2. “patient”

The ’507 patent states: “[t]he term ‘patient’ includes mammals and humans, particularly humans.” Ex. 1001, 5:63–64; *see also* Pet. 84; Reply 5. We preliminarily adopt this understanding of the term “patient.”

D. *Alleged Lack of Written Description Support*

Petitioner argues that the challenged claims lack written description support for two independent reasons.⁹ First, Petitioner contends that the Specification does not support the full scope of the claimed genus because it “does not disclose even a *single* example of the claimed subject matter, let alone sufficient species to support the extraordinarily broad genus that [Patent Owner] claimed.” Pet. 48; *see also id.* at 48–70. Second, Petitioner contends that the claims require administration of an aqueous formulation comprising carbidopa itself, but the Specification discloses only methods

⁹ In a footnote in its Reply, Petitioner posits a third written description challenge, namely that the claim 1 limitation reciting “the method is . . . without coadministration of a catechol-O-methyltransferase inhibitor” lacks written description support. Reply 4 n.2. Petitioner did not include this argument in the Petition, but asserts that the Federal Circuit’s decision in *Novartis Pharmaceuticals Corp. v. Accord Healthcare, Inc.*, 38 F.4th 1013 (Fed. Cir. 2022), which post-dates the Petition, “calls into question the support for the claims.” *Id.* We note, however, that Petitioner did not seek to address the *Novartis* decision when it requested authorization to file a Reply on August 23, 2022, two months after *Novartis* was decided on June 21, 2022. *See* Ex. 3001, 2. Because this belated argument is not responsive to any issue raised in Patent Owner’s Preliminary Response, we will not entertain it. 37 C.F.R. § 42.23(b).

and compositions comprising carbidopa prodrugs. *Id.* at 48. Patent Owner opposes. Prelim. Resp. 36–42.

For the reasons explained below, we find that Petitioner has met the threshold showing for post-grant review of claims 1–17 with respect to the first challenge (written description support for the claimed genus). On that basis, we institute post-grant review of all challenged claims. *See SAS Institute Inc. v. Iancu*, 138 S. Ct. 1348, 1358 (2018); 37 C.F.R. § 42.208(a) (“When instituting post-grant review, the Board will authorize the review to proceed on all of the challenged claims . . .”). We address this challenge first, then provide the parties guidance on Petitioner’s second written description challenge (support for carbidopa itself).

1. Legal Standards

35 U.S.C. § 112(a) requires that a patent’s specification “contain a written description of the invention . . . in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same.” *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). This provision ensures that as of the filing date “the inventor actually invented the invention claimed.” *Id.* at 1350–51. The test “requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.” *Id.* at 1351.

Adequate description of a genus requires “disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can ‘visualize or recognize’ the members of the genus.” *Id.* at 1350. “[F]unctional claim language can meet the written description

requirement when the art has established a correlation between structure and function.” *Id.*

2. *Alleged Lack of Support for the Claimed Genus*

Petitioner argues that the challenged claims encompass a broad genus of formulations functionally defined by the ability to achieve certain levodopa steady state plasma levels, but the Specification discloses neither a single operative species, nor sufficient representative species or common structural features, to support the breadth of the claims. Pet. 57–70.

Patent Owner responds that Petitioner “grossly exaggerates” the scope of the claims. Prelim. Resp. 39. Patent Owner also asserts that the Specification focuses on a closely-related group of phosphate prodrugs of levodopa and carbidopa, and, with respect to this “closely-related genus,” “Petitioner does not challenge that the specification provides a representative number of species within the scope of the genus and describes structural features common to the members of the genus.” Prelim. Resp. 39–40.

“[T]he level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology.” *Ariad*, 598 F.3d at 1351. Here, the claims are broad. As one example, the claims include levodopa prodrugs. *See supra* Section II.C.1. On this record, we credit Petitioner’s assertion that “[t]here are millions of potential different prodrugs of L-dopa” in different classes, including “(1) ester prodrugs; (2) amide prodrugs; (3) dimeric amide prodrugs; (4) carrier-mediated prodrugs; (5) glycosyl and peptide transport-mediated prodrugs; (6) chemical delivery systems; (7) phosphoramidate prodrugs; (8) cyclic prodrugs; and (9) co-drugs.” Ex. 1004 ¶ 71 (citing Exs. 1034, 1023); Pet. 58–59. As another

example, the claims “do not place any limits on the excipients that a skilled artisan might use” in the claimed formulations. Pet. 59. The claims also recite a functional requirement, i.e., the claimed method of continuously subcutaneously administering the formulation must achieve certain steady state levodopa plasma levels for certain periods of time. Pet. 57; Ex. 1004 ¶ 76.

The current record demonstrates that the relevant technology is complex and unpredictable. Pet. 59–63. Oral levodopa/carbidopa is the “gold-standard” for treatment of Parkinson’s disease, but it has shortcomings, including irregular absorption which can lead to wide fluctuation in levodopa plasma levels. Ex. 1003 ¶ 42; Prelim. Resp. 7. The record demonstrates that researchers considered continuous subcutaneous infusion of levodopa/carbidopa, but, given the low aqueous solubility at the required pH, they believed it was impossible to solubilize sufficient amounts of the drugs to achieve effective infusion. Ex. 1003 ¶¶ 47–50; Ex. 1013, 473; Ex. 1014, 340. Prior to October 2014 (the earliest possible priority date for the challenged claims), only one solution to this problem had been reported, namely ND0612, a levodopa/carbidopa formulation for continuous subcutaneous administration. Ex. 1003 ¶¶ 48, 49.

The current record also reflects that prodrugs are “highly unpredictable, both generally and as to L-dopa specifically.” Pet. 60–61; Ex. 1004 ¶¶ 28–30, 74–75; Ex. 1024, 4763; Ex. 1035, 3518. For example, the Petition addresses several failed attempts at levodopa prodrugs. Pet. 62; Ex. 1004 ¶ 77; Ex. 1025 ¶ 13; Ex. 1037, 373. Additionally, skilled artisans knew that small changes in a prodrug’s structure could affect properties such as solubility and pharmacokinetics. Ex. 1004 ¶¶ 30, 52, 75. And plasma

levels resulting from a new formulation can be unpredictable. Pet. 62–63. The only way a skilled artisan could identify whether a claimed formulation meets the claimed levodopa plasma levels is to make and test it. *Id.*; Ex. 1003 ¶ 102; Ex. 1004 ¶ 76.

Against this backdrop, we find that Petitioner demonstrates that the Specification more likely than not insufficiently supports the claimed genus. For example, the Specification “does not include a single example of continuous subcutaneous administration of a formulation including carbidopa itself (as opposed to a carbidopa prodrug) and L-dopa or an L-dopa prodrug, salt or hydrate, much less one that achieves the claimed L-dopa plasma levels.” Pet. 64; Ex. 1003 ¶ 104; Ex. 1004 ¶ 79. The Specification also discloses “only a handful of L-dopa prodrugs among the millions that a skilled artisan might try to use in the claimed methods of continuous subcutaneous administration.” Pet. 64; Ex. 1004 ¶ 80; Ex. 1003 ¶ 105. Additionally, the Specification “provides no disclosure as to how a skilled artisan could overcome the[] solubility issues and get sufficient amounts of carbidopa (or L-dopa) into solution without using the specific disclosed phosphate prodrugs within Formulas (I) and (II).”¹⁰ Ex. 1004 ¶ 68; *see also id.* ¶¶ 66–68.

On this record we find that Petitioner is also likely to show that the Specification “does not identify any common structural features of the

¹⁰ Patent Owner suggests that Example 16 provides adequate description of how to get sufficient carbidopa into solution to disclose and enable the claimed method. *See* Prelim. Resp. 38. At this stage, Patent Owner’s attorney argument is not supported by citation to persuasive evidence of record, and thus this factual issue is best left for development on the full record at trial.

L-dopa prodrugs that might work in the claimed methods or identify any other characteristics of the formulation that will lead to the desired plasma levels.” Pet. 67; Ex. 1004 ¶ 84; Ex. 1003 ¶ 108. And as noted above, “[a] skilled artisan would not expect different classes of prodrugs of L-dopa to behave similarly, and would know that small changes in the structure of a prodrug, even within a general class of them, can make a big difference in the properties of the prodrug, including its solubility and pharmacokinetics.” Pet. 65–66; Ex. 1004 ¶¶ 30, 75. Petitioner is also likely to show that “the specification’s singular focus on L-dopa prodrugs fails to support the claims’ option of using L-dopa itself, or a salt or hydrate thereof.” Pet. 66.

On this record, Patent Owner’s arguments do not undermine Petitioner’s showing. Patent Owner contends that Petitioner “grossly exaggerates” the scope of the claims, and has not substantiated why a person of ordinary skill in the art “would interpret the scope of levodopa prodrugs mathematically—entirely divorced from the specification and without the benefit of their skill and experience in the development of pharmaceuticals.” Prelim. Resp. 39. Patent Owner also contends that, with respect to the phosphate prodrugs disclosed in the Specification, “Petitioner does not challenge that the specification provides a representative number of species within the scope of the genus and describes structural features common to the members of the genus.” *Id.* at 40. These arguments ignore the claim scope. During prosecution, Patent Owner itself broadly defined the claims to cover “*any* molecule with a levodopa core moiety,” which includes *any* levodopa prodrug. Ex. 1002, 1601 (emphasis added). Accordingly, the genus of levodopa prodrugs encompassed by challenged claims is far

broader than the genus of levodopa phosphate prodrugs disclosed in the Specification. *See, e.g.*, Ex. 1003 ¶ 99; Ex. 1004 ¶¶ 71–72.

In sum, on this record Petitioner has demonstrated that the Specification more likely than not fails to provide adequate written description support for the claimed genus, including because the Specification appears to lack a representative number of species falling within the claims or structural features common to formulations that will meet the claimed functional requirements. *See Ariad*, 598 F.3d at 1350.

3. *Alleged Lack of Support for Methods Covering Administration of Carbidopa Itself*

Petitioner separately argues that because the Specification “exclusive[ly] focus[es] on a closely-related group of phosphate **prodrugs** of carbidopa,” it fails to show that the inventors invented the claimed method using a formulation that comprises carbidopa itself (as opposed to a carbidopa prodrug). Pet. 48.

On this record we agree with Petitioner that the Specification generally focuses on the use of carbidopa prodrugs, not carbidopa itself, in the disclosed methods and compositions. *See, e.g.*, Pet. 49–57, 21–27. For example, as outlined by Petitioner’s declarants, the Specification, including the Abstract, Field of the Invention, Summary of the Invention, and Detailed Description of the Invention sections, focuses on phosphate prodrugs of levodopa and carbidopa. Ex. 1003 ¶¶ 55–66, 88–97; Ex. 1004 ¶¶ 42–55, 63–65. Additionally, the Specification contains no example that involves administration of an aqueous formulation comprising carbidopa itself with “a compound comprising levodopa.” Ex. 1003 ¶ 90.

Patent Owner responds that there is “clear disclosure in the specification contemplating the use of carbidopa itself in the claimed inventions.” First, Patent Owner states that the “objective of the ’507 patent was to develop ‘[s]table, more highly concentrated, and/or less viscous formulations comprising L-dopa and/or *carbidopa* (or compounds capable of in vivo bioconversion to L-dopa and/or carbidopa).’” Prelim. Resp. 37 (quoting Ex. 1001, 2:44–47 (emphasis Patent Owner’s)). The quoted language, however, comes from the “Background of the Invention” section of the Specification, and the full sentence indicates that the recited formulations “are desirable.” Ex. 1001, 2:44–47. On this record, this language in context happens to mention carbidopa, but does not appear to be characterizing or identifying the invention. Indeed, both the “Field of the Invention” and “Summary of the Invention” sections of the Specification call out carbidopa prodrugs, but not carbidopa itself. *See id.* at 1:17–25, 3:1–4:5; *see also* Ex. 1004 ¶ 42 (explaining that Formula (I) represents a genus of carbidopa phosphate prodrugs).

Patent Owner next cites Examples 16 and 19 of the Specification, which show subcutaneous administration of carbidopa in rats and mini-pigs. Prelim. Resp. 37–38 (citing Ex. 1001, 82:37–83:43, 85:58–86:46). According to Patent Owner, the examples “demonstrate that prodrugs *and carbidopa* perform well upon administration—permitting either the prodrugs or carbidopa itself to be used in the claimed methods.” Sur-reply 4.

On this record we find that Petitioner has the better interpretation of these Examples: they show administration of carbidopa as a control to evaluate the purportedly novel prodrugs. *See* Pet. 50–51; Ex. 1003 ¶¶ 58, 91–93; Ex. 1001, 7:13–17. For example, Example 16 states: “For

comparison, a rat pharmacokinetics study with L-dopa and carbidopa was conducted to help assess the in vivo conversion of the prodrugs.” Ex. 1001, 82:34–83:43. In the context of the entire Specification, there is little to signal to a person of ordinary skill in the art that the use of carbidopa as a comparator means that formulations containing carbidopa itself are part of the invention. For example, there is no disclosure in the examples or elsewhere in the Specification that the carbidopa was administered together with a compound comprising levodopa, nor do Examples 16 and 19 disclose any steady state levodopa plasma levels following administration of such a formulation, as required by the claims. Pet. 51; Ex. 1003 ¶¶ 58, 61, 91–93. Additionally, even if the examples would have rendered obvious the use of carbidopa itself in the claimed methods, “a description that merely renders the invention obvious does not satisfy the requirement.” *Ariad Pharms., Inc.*, 598 F.3d at 1352 (citation omitted).

Patent Owner also points to disclosure indicating that the inventive methods comprise use of a “carbidopa prodrug ‘and/or’ levodopa prodrug,” and that the dose of the carbidopa prodrug may be “0 mg.” Prelim. Resp. 38–39 (citing Ex. 1001, 1:20–22, 17:23–30, 38:57–63). Patent Owner appears to be suggesting that because the invention does not require use of a carbidopa prodrug, a person of ordinary skill in the art would know that carbidopa itself can be used instead. On this record, however, we fail to see anything that would cause a person of ordinary skill in the art to link the cited disclosures—which do not mention carbidopa itself—to the use of carbidopa itself. Indeed, the section of the Specification titled “Co-Administration and/or Add-on Therapy” does not appear to suggest the addition of carbidopa itself. Ex. 1001, 41:61–42:36.

Although on this record we generally agree with Petitioner that the Specification has shortcomings with respect to disclosure relating to the use of carbidopa itself in the claimed method, we make an important observation regarding the parties' written description analyses. Both Petitioner and Patent Owner point to excerpts of the issued '507 patent to support their written description arguments. *See generally* Pet. 49–52; Prelim. Resp. 37–39. Written description support, however, is evaluated based on the originally-filed disclosure, which includes the original claims. *See, e.g., Mentor Graphics Corp. v. EVE-USA, Inc.*, 851 F.3d 1275, 1297 (Fed. Cir. 2017) (“Original claims are part of the original specification and in many cases will satisfy the written description requirement.”); *Ariad Pharm., Inc.*, 598 F.3d at 1349.

Petitioner asserts that “the specification of the '507 patent [is] substantively unchanged from the first non-provisional application filed in October 21, 2015.” Pet. 49. This statement, however, overlooks the applicant's preliminary amendment filed on May 4, 2020 (the filing date of the '400 application).¹¹ “A preliminary amendment that is present on the filing date of an application is part of the original disclosure of the application.” *See* 37 C.F.R. § 1.115(a)(1) (2019). As indicated above (*see supra* Section I.D), original claim 37 recited the use of carbidopa itself in the claimed method: “the L-amino acid decarboxylase inhibitor is **carbidopa** or a carbidopa prodrug.” Ex. 1002, 2–3 (emphasis added). Both parties mention the preliminary amendment (*see* Pet. 54; Prelim. Resp. 11), but do

¹¹ The pages of this preliminary amendment are scattered throughout Exhibit 1002. The consecutive pages can be found in Exhibit 1002 at 2 (page 1), 535–36 (pages 2–3), and 3–5 (pages 4–6).

not meaningfully address the impact, if any, of claim 37 on Petitioner’s written description argument. *See, e.g., Crown Packaging Tech., Inc. v. Ball Metal Beverage Container Corp.*, 635 F.3d 1373, 1381 (Fed. Cir. 2011) (finding that the original claims “show . . . that the applicants had in mind the invention as claimed”).

We encourage the parties to timely address in subsequent briefing the impact, if any, of claim 37 on Petitioner’s written description argument.

4. *Conclusion*

For the above reasons, on this record we determine that Petitioner has shown that claims 1–17 more likely than not lack adequate written description for the claimed genus. On that basis, we institute a post-grant review of all challenged claims.

E. Alleged Lack of Enablement

Petitioner asserts that claims 1–17 are unpatentable for lack of enablement because a person of ordinary skill in the art could not practice the claimed subject matter without undue experimentation. Pet. 70–79. Patent Owner opposes. Prelim. Resp. 36–42.

We find that Petitioner has met the threshold showing for post-grant review of claims 1–17 with respect to its enablement challenge, and thus this argument provides another basis for institution of a post-grant review of all challenged claims.

1. *Legal Standard*

A patent’s specification must describe the invention and “the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.” 35 U.S.C.

§ 112(a). The enablement requirement asks whether “the specification teach[es] those in the art to make and use the invention without undue experimentation.” *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). In analyzing undue experimentation, we consider factors such as: “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” *Id.*

2. *Analysis and Conclusion*

Petitioner walks through the *Wands* factors, reiterating arguments and evidence discussed above in Section II.D.2 regarding written description support for the claimed genus. Pet. 72–76; *see also* Ex. 1004 ¶¶ 86–95; Ex. 1003 ¶¶ 110–21. For example, Petitioner reiterates that the claims are broad, the field is unpredictable, and the Specification fails to disclose any operative species within the scope of the claims or provide guidance on successfully achieving the claimed levodopa steady state plasma levels with the claimed formulations. *See, e.g.*, Pet. 72–76; Ex. 1004 ¶¶ 71–77, 86–95; Ex. 1003 ¶¶ 110–20. Petitioner also asserts that there is “no teaching in the specification how a skilled artisan could get sufficient carbidopa or L-dopa into solution, given their low solubility, without the use of prodrugs.” Pet. 75; *see also* Ex. 1003 ¶¶ 68, 92, 94; Ex. 1004 ¶¶ 48, 96, 117.

As to the quantity of experimentation needed, Petitioner reiterates that “the only way that a skilled artisan could determine if formulations within the scope of the claims were capable of achieving the claimed steady state L-dopa plasma levels would be to make the formulations and test them,” and

asserts that it would take one year to design, synthesize, and test a levodopa prodrug candidate, plus more time to develop and test a formulation to determine the steady state levodopa plasma levels. Pet. 76 (citing Ex. 1004 ¶ 94).

For largely the same reasons discussed above in our written description analysis (*see supra* Section II.D.2), we find that Petitioner’s arguments regarding lack of enablement meet the standard for institution. Patent Owner’s one-paragraph retort does not presently undermine Petitioner’s showing. Prelim. Resp. 40. For example, Patent Owner contends that Petitioner exaggerates the breadth of the challenged claims, “particularly the genus of levodopa prodrugs.” *Id.* Patent Owner, however, does not grapple with Dr. Okun’s prosecution declaration, which broadly defined the claim term “a compound comprising levodopa” as including “*any* molecule with a levodopa core moiety, including . . . prodrugs.” Ex. 1002, 1601 (emphasis added); Prelim. Resp. 17 (advocating for adoption of Dr. Okun’s definition). This declaration did not place any limits on the included prodrugs. Patent Owner also argues that the Specification discloses examples of using carbidopa itself, but does not presently contest that the Specification lacks a working example comprising a combination of carbidopa and levodopa or a levodopa prodrug, let alone one that achieves the claimed levodopa plasma levels. Prelim. Resp. 17. Nor does Patent Owner presently contest the bulk of Petitioner’s other enablement arguments.

We determine on this record that Petitioner has shown that claims 1–17 more likely than not lack enablement. We emphasize, however, that

the question of enablement is a highly fact-dependent analysis, and any final decision on enablement will be based on the full trial record.

F. Alleged Anticipation by Yacoby-Zeevi and Obviousness Over Yacoby-Zeevi and Nyholm

Petitioner asserts that (1) claims 1–5 and 13–17 are unpatentable as anticipated by Yacoby-Zeevi; and (2) claims 1–17 are unpatentable as obvious over Yacoby-Zeevi and Nyholm. Pet. 79–105. Patent Owner contends that Petitioner has not demonstrated that Yacoby-Zeevi is prior art, but does not otherwise address the merits of Petitioner’s anticipation and obviousness arguments. Prelim. Resp. 59–83.

To provide the parties guidance, we supply reasons for our finding that Petitioner has sufficiently shown for purposes of institution that Yacoby-Zeevi is prior art. We also raise questions regarding the merits of Petitioner’s anticipation and obviousness challenges.

1. Legal Standards

To anticipate under 35 U.S.C. § 102, each and every claim element, arranged as in the claim, must be found in a single prior art reference. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359 (Fed. Cir. 2008). It is permissible to consider not only the literal teachings of an alleged anticipatory prior art reference, but also the inferences a person of ordinary skill in the art would draw from the reference. *Eli Lilly and Co. v. Los Angeles Biomedical Res. Inst.*, 849 F.3d 1073, 1074–75 (Fed. Cir. 2017).

A claim is unpatentable as obvious under 35 U.S.C. § 103 “if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the

art.” 35 U.S.C. § 103; *see also KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved based on underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) any objective indicia of nonobviousness. *Graham*, 383 U.S. at 17–18. An obviousness determination requires finding a reason to combine accompanied by a reasonable expectation of achieving what is claimed in the challenged patent. *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016). “[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *KSR*, 550 U.S. at 419–20.

Regarding whether Yacoby-Zeevi qualifies as prior art, at the institution stage, the Petition must identify evidence sufficient to establish it is more likely than not that the reference was publicly accessible before the critical date of the challenged patent. *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 at 13 (PTAB Dec. 20, 2019) (precedential) (“*Hulu*”).

A reference is “publicly accessible” if “persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence[] can locate it.” *SRI Int’l, Inc. v. Internet Sec. Sys., Inc.*, 511 F.3d 1186, 1194 (Fed. Cir. 2008). “[T]he standard for public accessibility is one of reasonable diligence, to locate the information by interested members of the relevant public.” *GoPro, Inc. v. Contour IP Holding LLC*, 908 F.3d 690, 695 (Fed. Cir. 2018) (internal quotations and citations omitted). In the

context of determining public accessibility of materials distributed at conferences, we consider factors including the expertise of the target audience, the nature of the conference or meeting, whether there were restrictions on public disclosure of the information, expectations of confidentiality, and expectations of sharing the information. *Id.* at 694. A determination whether a particular reference qualifies as prior art is “approached on a case-by-case basis.” *In re Hall*, 781 F.2d 897, 899 (Fed. Cir. 1986).

2. *Overview of Yacoby-Zeevi (Ex. 1005)*

Yacoby-Zeevi, an undated poster titled “Maintenance of Constant Steady State Therapeutic Plasma Concentrations of Levodopa Following Its Continuous Subcutaneous Administration with Carbidopa,” discloses a study investigating the effect of continuous subcutaneous administration of ND0612, a levodopa and carbidopa formulation, on the pharmacokinetics of levodopa. Ex. 1005.

Yacoby-Zeevi states that for patients with advanced Parkinson’s disease, levodopa fluctuations during oral administration result in “wearing-off between doses and dyskinesias.” *Id.* It also states that although “marked clinical improvements (reduced dyskinesias and ‘off’ periods) can be achieved from LD treatment by continuous intravenous or intraduodenal infusion,” these delivery options are inconvenient. *Id.* The poster explains that “[f]or this reason, we investigated the effect of continuous subcutaneous delivery of LD/CD formulations, ND0612, on the PK [pharmacokinetics] of LD.” *Id.*

According to Yacoby-Zeevi, pigs were continuously administered ND0612 at several concentrations and rates via an insulin pump for 24 to 46

hours. *Id.* “Venous blood samples were collected at pre-determined time points and plasma LD and CD concentrations were measured.” *Id.* The poster provides several graphs of the resulting pharmacokinetic data, and concludes that “SC delivery of solubilized LD and CD is a promising option for enhancing consistency of plasma LD concentrations.” *Id.*

3. *Overview of Nyholm (Ex. 1006)*

Nyholm, titled “Pharmacokinetics of Levodopa, Carbidopa, and 3-*O*-Methyldopa Following 16-hour Jejunal Infusion of Levodopa-Carbidopa Intestinal Gel in Advanced Parkinson’s Disease Patients,” discloses a pharmacokinetic study in Parkinson’s Disease patients wherein the patients were administered levodopa-carbidopa intestinal gel (“LCIG”). Ex. 1006, 316 (Abstract). LCIG “is a carboxymethylcellulose aqueous gel delivered directly to the proximal jejunum via a percutaneous endoscopic gastrojejunostomy (PEG-J) tube connected to a portable infusion pump.” *Id.* at 317 (citations omitted). Although not yet approved in the United States at the time of Nyholm’s publication, LCIG was “approved for use in more than 40 countries under the name Duodopa®.” *Id.*

In Nyholm’s study, “[i]ndividually optimized dosing of LCIG was delivered over a 16-h period, administered as a morning bolus followed by continuous infusion and, if needed, intermittent extra doses.” *Id.* Nyholm reports various pharmacokinetic parameters for levodopa, carbidopa, and a levodopa metabolite, 3-*O*-methyldopa (“3-OMD”). *Id.* at 320, Table II, Fig. 2.

Nyholm states that “LGIG was found to be safe and well tolerated,” and concludes that “jejunal infusion of LCIG results in low fluctuations in levodopa concentrations over the majority of the 16-h infusion duration in

advanced Parkinson’s disease patients.” *Id.* at 322. According to Nyholm, “[s]table plasma levodopa concentrations during LCIG administration may result in more consistent dopaminergic stimulation in the brains of PD [Parkinson’s Disease] patients and subsequent improvement in clinical symptoms.” *Id.*

4. *Analysis*

a) *Whether Yacoby-Zeevi is Prior Art*

Petitioner asserts that Yacoby-Zeevi is prior art under 35 U.S.C. § 102(a)(1) because (1) it “was published on NeuroDerm’s website at least by August 5, 2013,” and (2) Dr. Peter LeWitt presented the Yacoby-Zeevi poster on June 19, 2012, in Dublin, Ireland at the Movement Disorder Society’s Sixteenth International Congress of Parkinson’s Disease and Movement Disorders (“MDS Conference”). Pet. 4–6 (citing, e.g., Ex. 1007; Ex. 1003 ¶¶ 122, 124). Patent Owner disputes Petitioner’s contentions. Prelim. Resp. 59–82.

(1) *Publication on NeuroDerm’s Website*

According to Petitioner, Yacoby-Zeevi was published on NeuroDerm’s website as of August 5, 2013, as evidenced by its capture by the Wayback Machine, an internet crawler. Pet. 4 (citing Ex. 1007, 1–2). Patent Owner responds that Petitioner’s Wayback Machine evidence shows only “one instance of *technical* accessibility of Yacoby-Zeevi” by a web crawler, which does not indicate accessibility to a person of ordinary skill in the art. Prelim. Resp. 75; *see also id.* at 76–77, 78.

On this record, Patent Owner has the better argument. Petitioner’s evidence at most suggests that Yacoby-Zeevi was on NeuroDerm’s website as of August 5, 2013. *See* Ex. 1007. While this made Yacoby-Zeevi

“technically accessible,” i.e., “someone could theoretically [have found] it on the Internet,” “public accessibility requires more than technical accessibility.” *Samsung Elecs. Co. v. Infobridge Pte. Ltd.*, 929 F.3d 1363, 1369 (Fed. Cir. 2019) (quoting *Acceleration Bay, LLC v. Activision Blizzard Inc.*, 908 F.3d 765, 773 (Fed. Cir. 2018)); *see also* Prelim. Resp. 78–79. The record lacks, for example, any indication that the website was meaningfully indexed or cataloged, or some other evidence that “a person of ordinary skill in the art could have reasonably found the website and then found the reference on that website.” *See id.*

Petitioner’s responsive arguments are unavailing. It argues that “[p]rior art obtained via the Wayback Machine® sets forth a *prima facie* case that the art was publicly accessible at the date and time provided in the time stamp.” Reply 6 (quoting Manual of Patent Examining Procedure (MPEP) § 2128.II.E). The MPEP, however, provides that the *prima facie* case can be rebutted, as Patent Owner has done here. Sur-reply 6 (citing MPEP § 2128.II.E). Patent Owner, for example, argues—and on this preliminary record we agree—that based on the lack of evidence of “links or other direction on the Internet for finding” Yacoby-Zeevi, “[a]ccessibility to a [person of ordinary skill in the art] cannot be inferred” from the Wayback Machine evidence. Prelim. Resp. 76, 78. Petitioner suggests that additional evidence will show that Yacoby-Zeevi “was available from a link merely two pages from NeuroDerm’s homepage.” Reply 7. Such evidence, however, is not of record, and we will not speculate as to what it may or may not show. Sur-reply 7.

(2) *Presentation at Conference*

Petitioner contends that Dr. LeWitt presented Yacoby-Zeevi publicly on June 19, 2012, at the MDS Conference. Pet. 5–6. Dr. LeWitt, a co-author of Yacoby-Zeevi, testifies that the poster was on display at the conference; attendees were free to photograph or take notes on the contents of the poster; and paper copies were available for dissemination. *Id.* (citing Ex. 1003 ¶¶ 122–24; Ex. 1008); Reply 7.

Patent Owner responds that Dr. LeWitt “appears to have an interest” in this IPR, and his testimony lacks corroboration and particularity. Prelim. Resp. 64; *see also id.* at 61–66. Patent Owner questions how many people observed the poster and how long it was displayed, and disputes that attendees were permitted to photograph the poster. *Id.* at 66–73; *see also In re Klopfenstein*, 380 F.3d 1345, 1349 (Fed. Cir. 2004).

On this record we find sufficient evidence to establish that Yacoby-Zeevi more likely than not was publicly accessible at the MDS conference before the critical date of the challenged patent, and therefore qualifies as prior art. *Hulu*, Paper 29 at 13. Dr. LeWitt’s testimony that the poster was available to the thousands of attendees of the MDS Conference appears to be consistent with the conference materials of record. Ex. 1003 ¶¶ 122–24; Ex. 1008, 5 (indicating 5,100 attendees at the MDS Conference); Ex. 1033, 4 (indicating Yacoby-Zeevi’s inclusion in a guided poster tour); Ex. 2033, 17 (indicating Yacoby-Zeevi’s inclusion in a poster viewing session). Dr. LeWitt also testifies (and on this record Patent Owner does not specifically dispute) that paper copies of Yacoby-Zeevi were available for dissemination at the MDS Conference. Ex. 1003 ¶ 124.

Accordingly, the information of record suggests that Yacoby-Zeevi was likely available to the relevant public before the earliest possible priority date for the challenged claims. This appears to be true even if photographs were prohibited and the number of attendees at the guided poster tour is unknown, given that the poster appears to have been available to attendees via multiple viewing opportunities and unrestricted paper copies. *See, e.g., GoPro, Inc.*, 908 F.3d at 695 (finding catalog to be a printed publication where it was disseminated without restrictions at a trade show). We acknowledge Patent Owner's allegations relating to Dr. LeWitt's credibility and alleged bias. On this preliminary record, however, we do not find these undeveloped allegations to undermine Petitioner's arguments. Patent Owner is free to explore these issues during trial, including via cross examination of Dr. LeWitt.

(3) Conclusion

Based on the totality of evidence currently of record, we find that Petitioner has established it is more likely than not that Yacoby-Zeevi was publicly accessible (at least at the MDS Conference) before the earliest possible priority date of the challenged claims, and thus that Yacoby-Zeevi qualifies as prior art.

b) Anticipation and Obviousness Analysis

As noted above, at this stage Patent Owner challenges the prior art status of Yacoby-Zeevi but does not otherwise address the merits of Petitioner's anticipation and obviousness arguments. Nevertheless, to provide the parties guidance, we supply reasons that give us pause as to whether Petitioner has met the threshold showing for post-grant review with respect to these challenges.

Our concerns focus on the preamble of challenged claim 1. “[A]s a general rule preamble language is not treated as limiting.” *Arctic Cat Inc. v. GEP Power Prods., Inc.*, 919 F.3d 1320, 1327 (Fed. Cir. 2019) (citations omitted). Exceptions arise where, for example, the preamble (1) “recites essential structure or steps”; (2) provides antecedent basis for terms in the claim body; or (3) was relied on during prosecution to distinguish the claimed invention from prior art. *Catalina Mktg. Int’l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002). “[A] preamble is not limiting ‘where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention.’” *Id.* (quoting *Rowe v. Dror*, 112 F.3d 473, 478 (Fed. Cir. 1997)).

Here, Petitioner appears to assume that the preamble is limiting, because it cites portions of Yacoby-Zeevi that purportedly disclose the preamble, and because the Petition does not expressly contend that the preamble (or any portion thereof) is non-limiting. *See* Pet. 84; *see also TomTom, Inc. v. Adolph*, 790 F.3d 1315, 1323–24 (Fed. Cir. 2015) (finding portion of preamble limiting). As such, for purposes of this Decision, we likewise assume that the preamble is limiting. Indeed, at a minimum, recitation of “a Parkinson’s disease patient” in the preamble appears to provide antecedent basis for later recitations of “the patient” in the claim’s body. *See* Ex. 1001, 114:30–43.

Petitioner asserts, and on this record we agree, that Yacoby-Zeevi’s pigs fall within the ’507 patent’s definition of “patient,” which includes “mammals.” Pet. 84 (citing Ex. 1001, 5:63–64); *see also supra* Section II.C.2 (claim construction). The Petition, however, is silent as to whether

Yacoby-Zeevi's pigs qualify as *Parkinson's disease* patients. Accordingly, assuming the preamble language reciting "a Parkinson's disease patient" is limiting, at this stage we are unable to conclude that Petitioner has adequately shown that Yacoby-Zeevi more likely than not discloses this limitation, because the Petition does not address the "Parkinson's disease" portion of the limitation. This concern affects not only Petitioner's anticipation arguments, but its obviousness arguments as well, because with respect to claims 1–5 and 14–17, Petitioner stands on its anticipation arguments and does not make separate obviousness arguments for these claims. Pet. 98. Additionally, its obviousness arguments for the remaining dependent claims fail to address this preamble language. *See id.* at 98–105.

For the above reasons, we have reservations regarding whether Petitioner has demonstrated that the challenged claims are more likely than not unpatentable as anticipated and/or obvious. We invite the parties to address at trial whether the preamble language reciting "a Parkinson's disease patient" is limiting, and if so, whether Petitioner has demonstrated that the cited references disclose that subject matter.

G. Discretionary Denial Under § 325(d)

The parties dispute whether the Board should discretionarily deny the Petition under 35 U.S.C. § 325(d). Prelim. Resp. 22–36, 42–59; Pet. 105–07; Papers 7, 8.

1. Legal Standard

Section 325(d) provides that the Director¹² may "reject the petition" if "the same or substantially the same prior art or arguments previously were

¹² The Board institutes trial on behalf of the Director. 37 C.F.R. § 42.4(a).

presented to the Office.” The Board analyzes this issue under a two-part framework:

- (1) whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office;
- and (2) if either condition of [the] first part of the framework is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH, IPR2019-01469, Paper 6, 8 (PTAB Feb. 13, 2020) (precedential) (“*Advanced Bionics*”).

In analyzing whether the same or substantially the same art or arguments were previously presented to the Office, we consider factors including: (i) the similarities and material differences between the asserted art and the prior art previously presented to the Office; (ii) the cumulative nature of the asserted art and the prior art previously evaluated by the Office; and (iii) the extent of the overlap between the arguments made before the Office and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art. *See id.* at 8–10.

In analyzing whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims, we consider factors including: (iv) the extent to which the asserted art was evaluated by the Office, including whether the prior art was the basis for rejection during examination; (v) whether Petitioner has pointed out sufficiently how the Office erred in its evaluation of the asserted prior art; and (vi) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of prior art or arguments. *See id.*

2. *Analysis*

a) *Petitioner's § 112 Arguments*

As discussed above, Petitioner asserts that the challenged claims are unpatentable under 35 U.S.C. § 112(a) as not enabled and lacking adequate written description support for the full scope of the claimed genus and for methods comprising use of carbidopa itself, as opposed to carbidopa prodrugs, in the claimed formulations. *See supra* Sections II.D, II.E. Patent Owner argues there is no material difference between these arguments and “the analysis the Examiner already performed.” Prelim. Resp. 29. In support, Patent Owner cites (1) the Examiner’s § 112(b) rejection of the claims for reciting “an L-amino acid decarboxylase inhibitor,” where the Specification discloses only carbidopa and carbidopa prodrugs of Formula (I) as such inhibitors; and (2) the Examiner’s consideration of the claim term “a compound comprising levodopa” and his suggestion that Patent Owner expressly define this term. *Id.* at 25–26 (citing Ex. 1002, 547, 623); *id.* at 28–29 (citing Ex. 1002, 1594). Patent Owner also more generally argues that the Examiner “repeatedly focused on scope, breadth, and disclosure issues” during prosecution, for example as illustrated by other § 112 rejections. *See id.* at 26 and n.5, n.6.

We begin by considering the Examiner’s § 112(b) rejection of the claims based on the term “an L-amino acid decarboxylase inhibitor.” *See* Ex. 1002, 547. The Examiner rejected the claims as “fail[ing] to correspond in scope” with what the inventors “regard as the invention” because the claims recite “non-limiting L-amino acid decarboxylase inhibitors . . . and non-limiting carbidopa prodrugs,” but the Specification discloses only carbidopa and carbidopa prodrugs of Formula (I). *See* Ex. 1002, 547 (citing

¶¶ 3, 7 of the original specification filed with the '400 application¹³). In a subsequent interview, the Examiner “suggested limiting the inhibitors to applicant’s invention to place the claims in condition for allowance.” *Id.* at 623. In response, the applicant changed the claim term “an L-amino acid decarboxylase inhibitor” to “carbidopa, or a pharmaceutically acceptable salt thereof.” *Id.* at 685.¹⁴

Based on the present record, one reasonable interpretation of this prosecution history is that the Examiner found sufficient disclosure to support using carbidopa in the claimed method. This supports Patent Owner’s argument that the Examiner previously considered the issues raised by Petitioner’s written description argument regarding support for carbidopa itself.

However, regarding Petitioner’s additional § 112 arguments (written description support for the claimed genus and lack of enablement), we do not see sufficient evidence that the Examiner considered the specific questions Petitioner raises. Although not dispositive, we note that the Examiner did not issue any rejections during prosecution for lack of written description or enablement under 35 U.S.C. § 112(a). Reply 1. Patent Owner does not persuade us that the Examiner’s suggestion that the applicant define the claim term “a compound comprising carbidopa,” or the Examiner’s

¹³ The original specification filed with the '400 application is located at Ex. 1002, 30–183.

¹⁴ The applicant’s claim amendment was made in a nine-page Response to Non-Final Office Action filed on September 1, 2020. The pages of this Response are scattered throughout Exhibit 1002. The consecutive pages can be found in Exhibit 1002 at 626 (page 1), 685–86 (pages 2–3), and 679–84 (pages 4–9).

general focus on “scope, breadth, and disclosure issues” during prosecution (including as evidenced by other § 112 rejections), means that the Examiner considered the same issues Petitioner raises regarding support for and enablement of the broadly claimed genus. *See, e.g.*, Prelim. Resp. 26, 28–29. On the present record we see no persuasive reason to interpret the Examiner’s suggestion that the applicant expressly define the claim term “a compound comprising levodopa” as meaning that the Examiner considered whether the Specification adequately supports the broad, functionally-defined genus. Nor are we persuaded that a general focus on or consideration of § 112 issues is sufficient to signal that the Examiner considered the same or substantially the same § 112 arguments Petitioner raises here.

*b) Petitioner’s Anticipation Argument Based on
Yacoby-Zeevi and Obviousness Argument Based on the
Combination of Yacoby-Zeevi and Nyholm*

There is no dispute that Yacoby-Zeevi and Nyholm were not before the Examiner. Pet. 4, 107; *see generally* Prelim. Resp. 44–53. Patent Owner argues, however, that “Petitioner’s asserted art (i.e., Yacoby-Zeevi and Nyholm) are cumulative of, or even less relevant than, the prosecution art.” Prelim. Resp. 83. We consider Patent Owner’s arguments regarding Yacoby-Zeevi and Nyholm in turn.

(1) Yacoby-Zeevi

Yacoby-Zeevi concerns a clinical study of ND0612 in pigs. Ex. 1005. Patent Owner argues that the Examiner considered “abundant” ND0612 art that is cumulative of, or more relevant than, Yacoby-Zeevi, including:

(1) Adar Abstract 2017¹⁵; (2) Adar Abstract 1337¹⁶; (3) Caraco Abstract 452¹⁷ and Caraco 452 Poster¹⁸; and (4) Caraco Abstract LBA26 and Caraco LBA26 Poster¹⁹. Prelim. Resp. 45; Sur-reply 5; *see also* Prelim. Resp. 46 (citing Ex. 1002, 761, 765).

Patent Owner does not persuade us that Yacoby-Zeevi is cumulative of the ND0612-related art that was before the Examiner. As to the Adar abstracts (items (1) and (2)), Patent Owner itself indicates “they are from

¹⁵ Adar et al., *Continuous Administration of Subcutaneous Levodopa/Carbidopa (ND0612) Demonstrated Comparable Levodopa Pharmacokinetics to Levodopa/Carbidopa Intestinal Gel (LCIG)*, *Neurology*, 88 Supplement 16 Abstract (2017) (Ex. 2020, “Adar Abstract 2017”).

¹⁶ Adar et al., *Pharmacokinetic Profile of Continuous Levodopa/Carbidopa Delivery when Administered Subcutaneously (ND0612) Versus Duodenal Infusion (Levodopa/Carbidopa Intestinal Gel)*, Seventeenth Int’l Congress of Parkinson’s Disease and Movement Disorders, June 2013, Sydney, Australia, Abstract 1337 (2017) (Ex. 2018, “Adar Abstract 1337”).

¹⁷ Caraco et al., *Constant Therapeutic Levodopa Plasma Concentrations Maintained by Continuous Subcutaneous Administration of ND-0612, a Novel Formulation of Levodopa/Carbidopa*, Seventeenth Int’l Congress of Parkinson’s Disease and Movement Disorders, June 2013, Sydney, Australia (Ex. 1002, 839, “Caraco 452 Abstract”).

¹⁸ Caraco et al., *Constant Therapeutic Levodopa Plasma Concentrations Maintained by Continuous Subcutaneous Administration of ND-0612, a Novel Formulation of Levodopa/Carbidopa*, Seventeenth Int’l Congress of Parkinson’s Disease and Movement Disorders, June 2013, Sydney, Australia (Ex. 1021, “Caraco 452 Poster”).

¹⁹ Caraco et al., *ND0612, a Novel Formulation of Levodopa/Carbidopa for Continuous, Subcutaneous Administration, Achieves Steady-State Levodopa Plasma Concentrations in Parkinson’s Disease Patients*, Seventeenth Int’l Congress of Parkinson’s Disease and Movement Disorders, June 2013, Sydney, Australia (Ex. 2006, “Caraco LBA26 Poster”).

2017, after the '507 patent's critical date." Prelim. Resp. 46 n. 7. On this basis alone, we disagree with Patent Owner that the Adar abstracts are more relevant than Yacoby-Zeevi. Unlike the Adar abstracts, Yacoby-Zeevi is alleged to have been publicly available before October 21, 2014, the earliest possible priority date of the challenged claims. Pet. 4–5; *see also supra* Section II.F.4.a.

As to the Caraco abstracts and posters (items (3) and (4)), Patent Owner asserts they are more relevant than Yacoby-Zeevi because: (a) they report clinical study data in humans, not pigs; (b) their data is more contemporaneous with the '507 patent, having been presented one year after Yacoby-Zeevi was allegedly presented; and (c) they contain complete dosing and pharmacokinetic information, whereas Yacoby-Zeevi's data is allegedly incomplete. Prelim. Resp. 49–52.

We are not persuaded by Patent Owner's arguments. Patent Owner's first argument (pig versus human studies) is unavailing, because pigs are within the scope of the challenged claims. Reply 5 (citing Ex. 1001, 5:63–64); *see also supra* Section II.C.2 (claim construction). And, even accepting Patent Owner's second and third arguments as true, they do not render the Caraco references more relevant than Yacoby-Zeevi. The studies disclosed in the Caraco LBA26 Abstract and Poster involved co-administration of Stalevo, a COMT inhibitor, whereas Yacoby-Zeevi's pig study did not. *See* Pet. 107; Ex. 1002, 837; Ex. 2006; Ex. 1005; Ex. 1003 ¶ 137. Thus, Yacoby-Zeevi is more relevant to the challenged claims, because the claims expressly recite a method "without co-administration of a [COMT] inhibitor." Ex. 1001, 114:42–43; *see also* Ex. 1002, 866–67 (prosecution

declarant distinguishing the Caraco LBA26 references from the claims because of the COMT inhibitor).

We acknowledge that Patent Owner disputes whether Yacoby-Zeevi's results were obtained "without a COMT inhibitor." Sur-reply 5; *see also* Prelim. Resp. 50 (arguing that Yacoby-Zeevi "omits" information regarding "whether a COMT inhibitor was co-administered"). Patent Owner provides no specific basis for this speculation, other than noting that Yacoby-Zeevi elsewhere reports "incomplete and self-contradictory pig data." Sur-reply 5. At trial, Patent Owner is free to develop any alleged inconsistencies in Yacoby-Zeevi's data. At present, however, we are not persuaded that alleged omissions and/or inconsistencies in Yacoby-Zeevi's data would have left a person of ordinary skill in the art unsure about whether Yacoby-Zeevi co-administered a COMT inhibitor. On this record, we find that given Yacoby-Zeevi's silence regarding a COMT inhibitor, a person of ordinary skill in the art would have understood that one was *not* administered. *See* Ex. 1003 ¶ 137 ("A skilled artisan would understand that, if the method disclosed in Yacoby-Zeevi included co-administration of a COMT inhibitor, such co-administration would have been disclosed in the poster, for example, in the Materials and Methods section or in the title.").

Turning to the Caraco 452 Abstract and Poster, unlike Yacoby-Zeevi, these materials are not alleged to disclose the plasma levels recited in challenged claim 1. Pet. 107. That is, Petitioner asserts that "Yacoby-Zeevi . . . discloses that its methods are 'sufficient to achieve a steady state levodopa plasma level of about 1000 ng/ml to about 5000 ng/ml in the patient for at least 8 hours,' as . . . required by claim 1." *Id.* at 88 (quoting challenged claim 1). Patent Owner does not assert that the Caraco 452

Abstract and Poster contains this information. Indeed, during prosecution, the applicant distinguished these materials by arguing they show “that levodopa plasma levels for ND0612 without a COMT inhibitor do not exceed 500 ng/ml.” Prelim. Resp. 48 (citing Ex. 1002, 866–68).

In sum, Patent Owner does not persuade us that Yacoby-Zeevi is the same or substantially the same as the art the Examiner considered, or that the ND0612 art the Examiner considered was more relevant than Yacoby-Zeevi.

(2) *Nyholm*

Patent Owner argues that Nyholm’s pharmacokinetic data is duplicative of data reported in the Specification, and that Petitioner uses Nyholm to make the same arguments the applicant already overcame during prosecution. Prelim. Resp. 53–56.

Patent Owner is correct that Figure 8 in the Specification and Figure 2(a) in Nyholm appear to be the same, such that the levodopa plasma concentrations Petitioner relies on in Nyholm were before the Examiner. *Compare* Ex. 1001, Fig. 8, *with* Ex. 1006, Fig. 2(a). However, Patent Owner does not persuade us that Petitioner’s arguments here overlap with arguments made and overcome during prosecution.

As part of its obviousness challenge, Petitioner argues that a skilled artisan would have been motivated to increase the ND0612 infusion rate reported in Yacoby-Zeevi to achieve the steady state levodopa plasma levels reported in Nyholm, which were achieved following administration of Duodopa. Pet. 99–103; Prelim. Resp. 54. Patent Owner asserts that it previously overcame a similar argument made by the Examiner, namely that a skilled artisan would have increased the infusion rate of ND0612 reported in Caraco Abstract LBA26 in order to achieve the claimed levodopa plasma

levels. Prelim. Resp. 54 (citing Ex. 1002, 761, 837). Patent Owner asserts that it overcame this argument by arguing that “the prior art taught away from increasing subcutaneous infusion rates because it increases the levels of 3-OMD—a compound associated with side effects.” *Id.* at 54–55 (citing Ex. 1002, 1589, 868).

We are not persuaded that Petitioner’s arguments sufficiently overlap with the arguments made and overcome during prosecution. The Examiner rejected the claims as obvious over Caraco Abstract LBA26, not Nyholm. *See* Ex. 1002, 761–63, 816–21. Patent Owner distinguished Caraco Abstract LBA26 on several bases inapplicable to Nyholm, including that the drug administration in the abstract included a COMT inhibitor, and that steady state was not achieved. *See, e.g.,* Ex. 1002, 778–79, 866–68, 1586–88. Moreover, it is not clear that the Examiner accepted Patent Owner’s argument that the prior art taught away from increasing the infusion rate. The Examiner stated that the obviousness rejection was withdrawn “due to the Oath and amendment filed 6/8/21.” Ex. 1002, 1613. The “Oath” is Dr. Okun’s second declaration, which defined the claim term “a compound comprising levodopa,” but did not proffer the teaching away argument. *Id.* at 1601–02. The “amendment filed 6/8/21” included a claim amendment, but also did not proffer the teaching away argument. *Id.* at 1595–600.

In sum, Patent Owner does not persuade us that Nyholm is the same or substantially the same as the art the Examiner considered, or that Petitioner uses Nyholm to make the same arguments the applicant already overcame during prosecution. Prelim. Resp. 54.

c) Conclusion

Patent Owner does not persuade us to deny the Petition under § 325(d). The art and arguments in the Petition largely are not the same as or substantially similar to the art and arguments previously presented to the Office. Accordingly, we find that § 325(d) is not sufficiently implicated such that its statutory purpose would be undermined by instituting on all challenges, and thus we decline to exercise our discretion to deny the Petition under § 325(d). *See* SAS Q&A's, Part D1, Effect of SAS on Future Challenges that Could Be Denied for Statutory Reasons (June 5, 2018).²⁰

III. CONCLUSION AND NOTICES

On the current record, Petitioner sufficiently shows that least one of the challenged claims is more likely than not unpatentable. We decline to exercise our discretion to deny the Petition under 35 U.S.C. § 325(d).

At this stage of the proceeding, the Board has not made a final determination regarding the patentability of any challenged claim. Thus, any conclusion reached in the foregoing analysis could change upon completion of the record.

The Board will deem forfeited any issue not raised in a timely response to the Petition, or as permitted in another manner during trial, even if asserted in the Preliminary Response or discussed in this Decision.

Nothing in this Decision authorizes Petitioner, in a manner not otherwise permitted by the Board's rules, to supplement the information pertaining to any ground advanced in the Petition.

²⁰ Available at https://www.uspto.gov/sites/default/files/documents/sas_qas_20180605.pdf.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 324(a), a post-grant review is instituted based on all grounds asserted in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 324(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this Decision.

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Patent 11,091,507 B2

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