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Paper 9
Entered: August 17, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MARINUS PHARMACEUTICALS, INC.,
Petitioner,

v.

OVID THERAPEUTICS, INC.,
Patent Owner.

PGR2023-00020
Patent 11,395,817 B2

Before JEFFREY N. FREDMAN, ZHENYU YANG, and TIMOTHY G. MAJORS, *Administrative Patent Judges.*

FREDMAN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Marinus Pharmaceuticals, Inc. ("Petitioner") filed a Petition (Paper 2, "Pet.") requesting post-grant review of claims 1–31 (the "challenged claims") of U.S. Patent No. 11,395,817 B2 (Ex. 1001, "the '817 patent"). Ovid Therapeutics, Inc. ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp."). Patent Owner "disclaimed claims 1-21 and 23-24 of the '817 patent under 35 U.S.C. § 253(a) in compliance with 37 C.F.R. § 1.321(a)." Prelim. Resp. 4 (citing Ex. 2001, 1).

For this proceeding, we consider only Petitioner's unpatentability contentions with respect to the remaining challenged claims—i.e., claims 22 and 25−31 of the '817 patent. *See* 37 C.F.R. § 42.207(e) ("No post-grant review will be instituted based on disclaimed claims.").

We have authority to determine whether to institute a post-grant review under 35 U.S.C. § 324. Institution of a post-grant review is authorized by statute when "the information presented in the petition . . . would demonstrate 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) (2018). Applying that standard on behalf of the Director (37 C.F.R. § 42.4(a)) and in consideration of the Petition, Preliminary Response, and the evidence of record, we determine that the information presented shows that it is more likely than not that Petitioner would prevail in establishing unpatentability of claims 22 and 25–31 of the '817 patent.

This decision to institute trial is not a final decision as to patentability of claims for which post-grant review is instituted. Our final decision will be based on the full record developed during trial.

II. REAL PARTIES-IN-INTEREST

Petitioner identifies Marinus Pharmaceuticals, Inc. as the real party-in-interest. Pet. 91. Patent Owner identifies Ovid Therapeutics, Inc. as the real party-in-interest. Paper 4, 1.

III. RELATED PROCEEDINGS

Petitioner states, regarding related matters, that they are "not aware of any disclaimers, reexamination certificates, other than the PGR petition." Pet. 91. Patent Owner states that "U.S. Patent No. 11,395,817 (the '817 patent) is not involved in any related litigation matters." Paper 4, 1.

IV. THE '817 PATENT

A. Background

The '817 patent issued July 26, 2022, from US application 17/024,127 filed Sept. 17, 2020. Ex. 1001, codes (45), (21), (22). The '817 patent is a continuation of US Application 16/789,709, filed Feb. 13, 2020 which is a continuation of US 16/447,300 filed June 20, 2019, which is a continuation of US 16/356,517 filed Mar. 18, 2019, which is a continuation of US 16/013,500 filed June 20, 2018, which is a continuation of US 15/673,737, filed Aug. 10, 2017, which claims the priority benefit of a provisional applications US 62/490,293 filed Apr. 26, 2017 and US 62/373,589 filed on Aug. 11, 2016. *Id.*, code (63), (60).

The '817 patent "provides pharmaceutical compositions and methods that may be used in applications of epileptic disorders, such as status epilepticus." Ex. 1001, 2:7–9. The '817 patent teaches "[s]tatus epilepticus is a condition in which seizures follow one another without recovery of consciousness between them. Accordingly, in embodiments, the disclosed

methods are used to treat subjects that would otherwise be resistant to one or more conventional therapies." *Id.* at 10:8–42.

The '817 patent teaches "[i]n embodiments, methods are provided for treating an epileptic disorder by administering ganaxolone to a patient in need thereof." *Id.* at 6:27–29. The '817 patent teaches "methods of treating an epileptic disorder wherein the patient is provided improvement of at least one symptom for more than 4 hours after administration of the pharmaceutical composition to the patient." *Id.* at 14:21–25. The '817 patent further explains that "[i]n embodiments, improvement of at least one symptom for more than, e.g., 8 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 24 hours after administration of the pharmaceutical composition to the patient is provided." *Id.* at 14:28–32.

B. Post-Grant Review Eligibility

As a threshold issue, we must determine whether the '817 patent is eligible for post-grant review. There are two requirements that must be met for post-grant review to be available. First, post-grant review is only available if the petition is filed within nine months of the issuance of the challenged patent. 35 U.S.C. § 321(c). Petitioner certifies that the petition was filed within nine months of the '817 patent's July 26, 2022 issue date on March 15, 2023. Pet. 3; Ex. 1001, code (45).

Second, post-grant review is available only for patents that issue from applications that at one point contained at least one claim with an effective filing date of March 16, 2013, or later. *See* Pub. L. No. 112-29, §§ 3(n)(1), 6(f)(2)(A). Here, the earliest priority date recited for the '817 patent is provisional application US 62/373,589 filed on August 11, 2016.

V. ILLUSTRATIVE CLAIMS

Claims 22 and 25 are illustrative of the remaining challenged claims in the '817 patent, and are reproduced below. Because claims 22 and 25 depend from claim 21 (now disclaimed), we also include claim 21 below for necessary context.

> 21. A method of treating status epilepticus comprising administering to a patient in need thereof a pharmaceutical composition comprising ganaxolone or a pharmaceutically acceptable salt thereof wherein the pharmaceutical composition is administered intravenously.
>
> 22. The method of claim 21 wherein the pharmaceutical composition provides improvement to the patient after administration for more than 8 hours.
>
> 25. The method of claim 21 wherein the patient is administered about 500 mg to 1000 mg/day ganaxolone.

Ex. 1001, 40:9–21.

VI. ASSERTED GROUNDS

Petitioner contends that the challenged claims are unpatentable based on a number of grounds, several of which were mooted by Patent Owner's disclaimer of claims 1–21, 23, and 24 including Petitioner's grounds 5, 6, and 8. Pet. 4; Ex. 2001. The remaining grounds are presented below.

Ground	Reference(s)/Basis	35 U.S.C. §	Claim(s) Challenged
1	Zhang[1]	§ 102	22, 25–31
2	Zhang	§ 103	22, 25–31
3	Zhang, Saporito P1[2]	§ 103	22, 25–31

[1] Zhang et al., WO 2016/127170 A1, published Aug. 11, 2016. Ex. 1009.
[2] Saporito et al., *Ganaxolone Administered Intravenously Prevents Behavioral Seizures and Promotes Survival in the Rat Lithium-Pilocarpine*

	Saporito P2[3]		
4	Zhang, Marinus Orphan Drug Press Release,[4] Marinus Phase I Press Release[5]	§ 103	22, 25–31
7	Enablement	§ 112	22, 25–31

Petitioner also relies on the Declaration of Michael A. Rogawski, M.D. *See* Ex. 1003.

VII. 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 as of the effective filing date of the challenged claims. Petitioner contends that one of ordinary skill in the art would

> have had a medical degree, or a Ph.D. in pharmacology or other field related to the development of pharmaceuticals, or equivalent degree, and several years of experience as a

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Model of Status Epilepticus, Poster presented April 17, 2016 at the 2016 AAN Annual Meeting ("Saporito P1"). Ex. 1013.

[3] Saporito et al., *Intravenous Administration of Ganaxolone Attenuates Electroencephalographic Seizures in a Diazepam Resistant Model of Status Epilepticus*, Poster presented April 19 and April 20, 2016 at the 2016 AAN Annual Meeting ("Saporito P2"). Ex. 1014.

[4] *Marinus Pharmaceuticals Receives FDA Orphan Drug Designation for Ganaxolone IV to Treat Status Epilepticus*, Published April 15, 2016, Available at: https://ir.marinuspharma.com/news/news-details/2016/Marinus-Pharmaceuticals-Receives-FDA-Orphan-Drug-Designation-for-Ganaxolone-IV-to-Treat-Status-Epilepticus/default.aspx ("April 15, 2016, Press Release"). Ex. 1011.

[5] *Marinus Pharmaceuticals Doses First Subject in Phase I Clinical Trial for Ganaxolone IV*, Published on June 22, 2016, Available at: https://ir.marinuspharma.com/news/news-details/2016/Marinus-Pharmaceuticals-Doses-First-Subject-in-Phase-1-Clinical-Trial-for-Ganaxolone-IV/default.aspx ("June 22, 2016, Press Release"). Ex. 1022.

> practicing neurologist treating patients who suffer from seizure disorders including status epilepticus and/or several years of experience in researching treatments for such seizure disorders.

Pet. 33–34. Patent Owner, at this time, "does not dispute Petitioner's definition of a skilled artisan." Prelim. Resp. 23.

Because Petitioner's proposed level of ordinary skill in the art is undisputed and consistent with the cited prior art, we adopt it for purposes of this Decision.

VIII. CLAIM CONSTRUCTION

In a *post-grant* review, 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. § 42.200(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.*

Petitioner submits a construction for the term "patient." All remaining terms should be given their plain meaning.

> The '817 defines "patient" (used interchangeably with "subject") as "includ[ing], but not limited to, primates such as humans, canines, porcine, ungulates, rodents, poultry, and avian." One such patient within the scope of the Challenged Claims is, therefore, a rat. Another is a human.

Pet. 34–35 (citing Ex. 1001, 32:65–67; Ex. 1003 ¶ 67) (footnote omitted).

Patent Owner asserts "'[t]reating status epilepticus comprising administering to a patient in need thereof' in claims 22 and 25-31 means 'treating a human patient suffering from SE.' This construction is supported by the intrinsic record." Prelim. Resp. 27–28. Patent Owner contends that when claim 22 recites "a patient in need thereof," a "skilled artisan would

thus understand that the someone 'in need'" would be a human patient suffering from SE, and is not a rat or other animal receiving ganaxolone for research purposes." Prelim. Resp. 28. Patent Owner asserts the Specification "refers to 'treating' in the context of addressing *clinical* and *subclinical* symptoms of a disease or a condition, and not in the context of preclinical, research uses." Prelim. Resp. 28 (citing Ex. 1001, 29:29–51). Patent Owner asserts "for claims 25-31, a skilled artisan would understand that the doses recited in these claims (ranging from 500 mg to 1050 mg) are at least 130 times larger than the doses administered to rats in the '817 patent's examples and would likely kill a rat." Prelim. Resp. 29.

We find that on the present record, the evidence more likely than not supports Petitioner's claim interpretation which is based on the express definition of the term "patient" in the '817 patent specification. That express definition states: "'Patient' and 'subject' are used interchangeably herein and include, but not limited to, primates such as humans, canines, porcine, ungulates, rodents, poultry, and avian." Ex. 1001, 32:65–67.

> [T]he definition in the patent documents controls the claim interpretation. . . . Any other rule would be unfair to competitors who must be able to rely on the patent documents themselves, without consideration of expert opinion that then does not even exist, in ascertaining the scope of a patentee's right to exclude.

Southwall Tech., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1578 (Fed. Cir. 1995). "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005).

While a term in a Specification may be interpreted by implication, we are not persuaded by Patent Owner's attempt to infer a different construction that contradicts the express definition of "patient" and "subject" in the '817 patent. Patent Owner simply asserts that a skilled artisan would understand someone in need of treatment of status epilepticus to be solely a human patient, and provides no evidentiary basis to exclude veterinary uses of the compound, particularly when the '817 patent expressly defines the term "patient" to include such veterinary patients.

As to Patent Owner's reliance on the terms "clinical" or "subclinical" to infer treatment only of humans, we find no persuasive reason or evidence explaining why treatment of animals is excluded by these terms. Patent Owner does not, on this record, identify any discussion of any understanding the Examiner inferred from the prosecution history or any indication that the prosecution history disagrees with the express definition of "patient" in the Specification. Moreover, the terms "clinical" and "subclinical" do not appear in claims 21, 22, or 25–31.

Lastly, as to the dosing in claims 25–31, Patent Owner simply asserts without any evidentiary foundation on this record that these doses "would likely kill a rat." We do not find this argument persuasive on this record as it lacks evidentiary support.

We determine that we need not expressly construe any other claim terms for the purpose of deciding whether to institute post-grant review. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("[W]e need only construe 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 above. Any final claim constructions will be based on the full trial record.

IX. 325(d) – DISCRETION TO DECLINE TO INSTITUTE

Petitioner asserts "it is clear from the prosecution history that neither the art nor the arguments presented were properly considered, or, in some cases, even considered at all." Pet. 82. Petitioner asserts "the Examiner explicitly *did not consider* some of the highly probative publications presented in the third party observations. Nor did the Examiner make a single anticipation or obviousness rejection during prosecution—over these or any other prior art publication(s)." *Id.* Petitioner asserts "[g]iven that the Examiner purportedly considered Zhang, which demonstrates an actual reduction to practice of this embodiment of claim 1, but did not make any anticipation or obviousness rejection over Zhang, either the Examiner overlooked Zhang's teachings, or made an error of law." *Id.* at 86 (footnote omitted). Lastly, Petitioner asserts "[d]uring prosecution, the Examiner did not have the benefit of the explanations provided in Dr. Rogawski's declaration. That additional evidence presented here with the Petition is another reason why discretionary denial is not appropriate here." *Id.* at 89.

Patent Owner urges us to decline to institute the asserted grounds under 35 U.S.C. § 325(d) "because Zhang, the primary reference Petitioner relies on, was undoubtedly presented to and considered by the Office during examination of the '817 patent." Prelim. Resp. 76. Patent Owner asserts

"Zhang was first disclosed to the Office in a January 6, 2021 IDS submitted by the applicant. *See* Ex. 1002, 19 (WO 2016127170). Zhang was again submitted to the Office in a February 8, 2021 Third-Party Submission filed by Robert H. Underwood of Hogan Lovells US LLP." *Id.* (citing Ex. 1002, 38). Patent Owner notes "the Examiner signed the Third-Party Submission indicating that the Examiner had considered all references included with the submission, including Zhang. Ex. 1002, 95-96." *Id.* at 77.

Patent Owner asserts "none of the asserted references discloses or suggests an improvement of SE treatment for 8 hours after ganaxolone administration, as required by claim 22. And the dose ranges in the prior art do not disclose or suggest the doses recited in claims 25-31 with sufficient specificity." Prelim. Resp. 79. Patent Owner asserts the Examiner "issued multiple office actions with obviousness, enablement, and double patenting rejections (*see* Exs. 1026, 1027). This demonstrates that the Examiner had acquired familiarity with the use of ganaxolone for epilepsy treatment and with the relevant prior art in that field." *Id.* at 80. Patent Owner asserts "Dr. Rogawski's declaration also does not establish Examiner error." *Id.*

1. *Principles of Law*

Institution of post-grant review, like *inter partes* review, is discretionary. *Harmonic Inc. v. Avid Tech, Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (explaining that "the PTO is permitted, but never compelled, to institute an IPR proceeding"). The Patent Office may, for example, deny institution under 35 U.S.C. § 325(d), which provides, in pertinent part, that "[i]n determining whether to institute or order a proceeding under this chapter . . . the Director may take into account whether, and reject the

petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office."

In evaluating whether the same or substantially the same prior art or arguments were previously presented to the Office, the Board has identified several non-exclusive factors for consideration. *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first paragraph) ("the *Becton, Dickinson* factors"). Those factors are as follows:

> (a) the similarities and material differences between the asserted art and the prior art involved during examination;
>
> (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
>
> (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
>
> (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;
>
> (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
>
> (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Id. (footnote omitted); *see also* Patent Trial and Appeal Board Consolidated Trial Practice Guide (Nov. 2019)[6] 62–63.

As explained in *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (PTAB

[6] Available at https://www.uspto.gov/TrialPracticeGuideConsolidated

Feb. 13, 2020) ("*Advanced Bionics*") (precedential), we further apply the following two-step framework in determining whether discretionary denial under § 325(d) is appropriate:

> (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.

Becton, Dickinson Factors (a), (b), and (d) relate to the first step, and *Becton, Dickinson* Factors (c), (e), and (f) relate to the second step. *Id.* Only if the same or substantially the same art or arguments were previously presented to the Office do we then consider whether petitioner has demonstrated error. *Advanced Bionics*, at 8–10. "If the petitioner fails to show that the Office erred, the Director may exercise [her] discretion not to institute *inter partes* review." *Id.* at 8–9 ("If a condition in the first part of the framework [i.e., substantially same art or arguments] is satisfied and the petitioner fails to make a showing of material error, the Director generally will exercise discretion not to institute *inter partes* review."). "At bottom, this [§ 325(d)] framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown." *Id.* at 9. An "example of a material error" could be "misapprehending or overlooking specific teachings of the relevant prior art where those teachings impact patentability of the challenged claims." *Id.* at 8 n.9

2. *Analysis*

Under the first step of the *Advanced Bionics* framework, we must determine whether the same or substantially the same prior art was previously presented to the Office. *Advanced Bionics*, at 8. Patent Owner observes that Zhang was before the Examiner in an Information Disclosure Statement ("IDS"). Prelim. Resp. 76–77 (Ex. 1002, 19, 38). Petitioner does not dispute that Zhang was made of record. Pet. 86.

Thus, Zhang was "previously presented to the Office." *See Advanced Bionics*, at 7–8 ("Previously presented art includes . . . art provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent."). We note that Petitioner here presents not only Grounds 1 and 2 (relying on Zhang), but also Grounds 3 and 4, which address all challenged claims and rely on Zhang in combination with other prior art. We recognize that in this situation, where the petition includes grounds with additional prior art that is not the same as or cumulative of previously presented prior art, there is discretion to find that these combinations support finding that the same or substantially the same prior art was not previously presented. *See, e.g.*, *Halliburton Energy Servs., Inc. v. U.S. Well Servs., LLC*, IPR2021-01036, Paper 12 at 19–20 (PTAB Jan. 19, 2022). As Zhang was previously presented to the Office, we proceed to the second step of the *Advanced Bionics* framework.

Under the second step of the *Advanced Bionics* framework, we must determine whether Petitioner has demonstrated Examiner error in a manner material to the patentability of the challenged claims. *Advanced Bionics*, at

10. *Becton, Dickinson Factors* (c), (e), and (f) inform our analysis at this step. *Id.* at 8.

As to *Becton, Dickinson* Factor (c), "the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection," whether the prior art was the basis for a rejection is significant to this analysis. *Compare Boragen, Inc. v. Syngenta Participations AG*, IPR2020-00124, Paper 16 at 7–8 (PTAB May 5, 2020) (denying institution under § 325(d) where the primary reference and a secondary reference in the petition were the basis for five obviousness rejections during the prosecution of the patent at issue), *with DraftKings Inc. v. Interactive Games LLC,* IPR2020-01107, Paper 10 at 16 (PTAB Jan. 6, 2021) (declining to deny institution under § 325(d) where the primary reference in the petition was not the basis of a rejection and disclosed the limitations upon which the Examiner relied to allow the patent).

Here, Petitioner asserts Zhang was not the basis of any rejection, and Patent Owner does not identify any rejection based on Zhang, and there is no evidence that the Examiner meaningfully considered the relevant disclosures of Zhang. Pet. 86; Prelim. Resp. 80. We find unpersuasive Patent Owner's reliance on the Examiner's issuance of "multiple office actions with obviousness, enablement, and double patenting rejections (*see* Exs. 1026, 1027)" in related cases because the claims in these related cases were drawn to different conditions, CKDL5 deficiency disorders or PCDH19 related epilepsy, not status epilepticus as in the instant claim 22. *See* Prelim. Resp. 80 (*cf.* Ex. 1026, 27; Ex. 1027, 12). Thus, the patient populations at issue were different and therefore the prior art that was relevant to the claims at issue would also necessarily differ.

As to *Becton, Dickinson* Factor (e), "whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art," Petitioner provides persuasive evidence of Examiner error. *See* Pet. 36–39 (citing Ex. 1009, 21–27). We agree with Petitioner that the Examiner overlooked Zhang with regard to claim 1, now statutorily disclaimed by Patent Owner, and therefore "either the Examiner overlooked Zhang's teachings, or made an error of law." Pet. 86. Moreover, as will be explained more fully below, even if we solely consider claim 22 in this analysis, we find that, on the current record, the evidence sufficiently shows that claim 22 is anticipated by Zhang. We, thus, find that the Examiner erred by either overlooking, or failing to appreciate, the materiality of the disclosure of Zhang.

Finally, as to *Becton, Dickinson Factor* (f), "the extent to which additional evidence and facts presented in the Petition warrant reconsideration of prior art or arguments," Petitioner addresses Zhang as it relates to claims 22 and 25–31. Pet. 43–48. Petitioner also relies upon the Rogawski Declaration to support the analysis. Ex. 1003 ¶¶ 89–95, 99–105. The addition of an expert Declaration in this case that supports anticipation based on the inherency reasoning in claim 22 significantly adds evidence that was unavailable to the Examiner, even if the Examiner had reviewed Zhang.

Considering *Becton, Dickinson* Factors (c), (e), and (f) together, we conclude that Petitioner sufficiently demonstrates Examiner error based on the grounds in its Petition, with support from expert testimony, which shows, in particular, that the Examiner overlooked, or did not appreciate, the materiality of Zhang's disclosures relating to the claims at issue.

3. *Conclusion*

For the reasons discussed above, we conclude that the Petition presents facts and evidence that, in this case, sufficiently demonstrate the Examiner erred in a manner material to the patentability of the challenged claims, and we therefore decline to exercise our discretion to deny institution under 35 U.S.C. § 325(d).

X. ANALYSIS

A. Principles of Law

In a post-grant review, as in an inter partes review, "the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable." *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016). This burden of persuasion never shifts to Patent Owner. *See Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015).

"Determining whether claims are anticipated involves a two-step analysis. The first step involves construction of the claims of the patent at issue. Claim construction is a question of law reviewed *de novo*." *In re Aoyama*, 656 F.3d 1293, 1296 (Fed. Cir. 2011). "The second step [of an anticipation analysis] involves comparing the claims to the prior art. Anticipation is a question of fact reviewed for substantial evidence." *In re Aoyama*, 656 F.3d at 1296. "A prior art reference anticipates a patent claim under 35 U.S.C. § 102(b) if it discloses every claim limitation." *In re Montgomery*, 677 F.3d 1375, 1379 (Fed. Cir. 2012). A reference may anticipate inherently if a claim limitation that is not expressly disclosed "is necessarily present, or inherent, in the single anticipating reference." *Verizon*

Servs. Corp. v. Cox Fibernet Va., Inc., 602 F.3d 1325, 1337 (Fed. Cir. 2010).

We analyze the asserted grounds of unpatentability in accordance with these principles to determine whether Petitioner has met its burden to establish that it would more likely than not prevail at trial.

B. Overview of the Asserted Prior Art

1. *Zhang (Ex. 1009)*[7]

Zhang is a published patent application filed with the World Intellectual Property Organization on February 8, 2016 and published on August 11, 2016. Ex. 1009, codes (22), (43). Zhang discloses that "Status epilepticus (SE) is a serious seizure disorder in which the epileptic patient experiences a seizure lasting more than five minutes, or more than one seizure in a five minute period without recovering between seizures." Ex. 1009, 2 ¶ 1. Zhang teaches "[t]here are currently no good treatment options for these patients. The mortality rate for refractory status epilepticus (RSE) patients is high." *Id.* Zhang teaches "there exists the need for additional treatments for seizure disorders such as status epilepticus . . . This disclosure fulfills this need and provides additional advantages." *Id.,* 2 ¶ 4.

Zhang teaches "an injectable ganaxolone formulation comprising ganaxolone, sulfobutyl ether-β-cyclodextrin; and water. . . . The disclosure also provides a method of treating a patient having a seizure disorder . . . comprising administering an effective amount of the injectable ganaxolone formulation." Ex. 1009, 3 ¶ 6. Zhang teaches a "'patient' is a human or non-

[7] The pagination used herein follows that in Ex. 1009, not the original pagination of the document but the paragraph numbers are those of the original document.

human animal in need of medical treatment. Medical treatment includes treatment of an existing condition, such as a disorder." *Id.*, 5 ¶ 22. "Seizure disorders that may be treated with the substituted β-cyclodextrin-ganaxolone injectable formulation include status epilepticus." *Id.*, 13 ¶ 70. Zhang teaches embodiments where the

> substituted β-cyclodextrin-ganaxolone injectable formulation is administered as an intravenous infusion dose, either without or without a previous bolus dose for 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 consecutive days. The infusion dose may be administered at a rate of 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mg/kg/hr or in a range of about 1 mg/kg/hr to about 10 mg/kg/ hr or 2 mg/kg/hr to about 8 mg/kg/hrs.

Id., 14 ¶ 76.

Zhang provides a working example addressing ganaxolone effect on pilocarpine-induced status epilepticus in rats in Example 8. Ex. 1009, 21 ¶ 117. Zhang teaches a study to "determine the ability of a CAPTISOL-ganaxolone (GNX) formulation administered intravenously (IV) at 12 and 15 mg/kg to inhibit pilocarpine induced status epilepticus (SE). . . . In this study, test drugs were administered either 15 or 60 minutes after onset of SE and compared to vehicle (30% Captisol)." *Id.* Zhang teaches "[c]ortical EEG[8] activity was recorded in rats before and after administration of pilocarpine to induce SE. Animals were pre-treated with LiCl to enhance and improve reliability of seizure induction and scopolamine to reduce peripheral cholinergic side effects of pilocarpine." *Id.*, 21 ¶ 118. Zhang teaches "EEG activity was recorded for 5 h after SE onset, and

[8] "[B]rain waves are measured with an electroencephalogram [EEG]." Ex. 1001, 11:9–10.

anticonvulsant activity was assessed by determining changes in EEG power over frequency ranges from 0.3 to 96 Hz." *Id.* Zhang teaches the

> time of SE onset was determined by observation and recorded, and the animal dosed with the vehicle, allopregnanolone, or ganaxolone either 15 or 60 min post SE-Onset. Rats were observed for behavior changes at approximately 2, 15, 30, 60, 120 and 240 minutes after pilocarpine administration. Each animal was recorded once and euthanized 5 h after treatment.

Id., 24 ¶ 127. Zhang teaches "[g]anaxolone at 12 and 15 mg/kg produced qualitatively similar results, with both dose levels producing a very strong reduction in SE amplitude overall." *Id.*, 25 ¶ 134. Table 6 of Zhang, comparing treatment with the control (vehicle) and 15 mg/ml ganaxolone administered 15 minutes after status epilepticus onset is reproduced in part below.

TABLE 6 - Treatment Effects, Rats Treated 15 minutes post SE onset							
		Significance, Time post drug administration					
Comparison	Frequency	0-15 min.	15-30	30-60	1-2 hrs	2-3 hrs	3-5 hrs
Vehicle vs GNX (12 mg/ml) both administered 15 minutes post SE onset	0-5 Hz	****	****	****	****	***	**
	5-10 Hz	****	****	***	**	*	ns
	10-30 Hz	***	****	**	*	ns	ns
	30-50 Hz	***	***	**	*	ns	ns
	50-70 Hz	**	**	*	**	ns	ns
	70-96 Hz	**	**	*	**	ns	ns
Vehicle vs GNX (15 mg/ml) both administered 15 minutes post SE onset	0-5 Hz	****	****	****	****	****	***
	5-10 Hz	****	****	****	****	***	ns
	10-30 Hz	****	****	****	**	*	ns
	30-50 Hz	***	***	***	**	ns	ns
	50-70 Hz	**	**	**	**	ns	ns
	70-96 Hz	**	***	**	**	ns	ns

"TABLE 6 summarizes the treatment effects for allopregnanolone or ganaxolone administered 15 minutes post seizure onset." *Id.*, 25 ¶ 131. Table 6 shows that

> [w]hen dosed 15 minutes after SE-onset, GNX reduced EEG power across all frequency ranges to levels at or below baseline for at up to 5 h. From 5-70 Hz, EEG power was reduced to near the baseline level and remained there for 5 h post dosing. At 0-5

> Hz, EEG power was reduced below the baseline level for approximately 90 min, and at 70-96 Hz, EEG power remained below baseline for the entire 5 h.

Id., 25 ¶ 135.

2. *Saporito P1 (Ex. 1013)*

Saporito P1 is a poster presented at American Academy of Neurology 2016 Annual Meeting. Ex. 1012, 46. Saporito P1 teaches their "studies were conducted to evaluate the dose- and time-dependent therapeutic potential of intravenously, (IV) administered GNX for the treatment of CSE in this clinically translatable rodent model. Moreover, these studies measured behavioral seizures and survival, and complement studies that measured seizures by EEG activity." Ex. 1013, 1. Saporito P1 teaches "animals received GNX dose-levels of 6, 9, 12 mg/kg." *Id.* Saporito P1 teaches "[c]ompounds were administered via IV administration at time of CSE onset (time 0) and 15, 30, and 60 minutes after onset." *Id.* Saporito P1 teaches that "[a]fter compound administration, animals were observed for the presence or absence of convulsive seizures (stage 3 or greater) for an additional 2 hours. Animals that did not exhibit a convulsive seizure during that time period were considered protected." *Id.* Saporito P1 concluded that

> Lithium-pilocarpine administration produced a convulsive status epilepticus. . . . GNX IV halted CSE and produced a dose-dependent reduction in seizures associated with CSE when administered at 3 different doses over four separate time points after the first observed convulsive seizure. . . . Significant activity of GNX was observed at a dose of 6 mg/kg and maximal protection at dose levels between 9 and 12 mg/kg. . . . GNX IV promoted survival at rates similar to those observed with administration of allopregnanolone as measured at 24 hours after CSE onset in CSE induced rats.

Id.

3. *Saporito P2 (Ex. 1014)*

Saporito P2 is a poster presented at American Academy of Neurology 2016 Annual Meeting. Ex. 1012, 99. Saporito P2 teaches "current studies were designed to compare the anti-epileptic activity of GNX and ALLO in this treatment resistant model of SE." Ex. 1014, 1. Saporito P2 teaches "SE was first identified by presence of large amplitude slow wave EEG activity and then behaviorally using the Racine scale. Racine stage 3 seizures were used as the time-marker for SE onset and subsequent treatment." *Id.* Saporito P2 teaches "GNX, ALLO, or diazepam were administered via intravenous (IV) bolus injection 15 or 60 minutes after detection of SE onset." *Id.* Saporito P2 teaches

> Ganaxolone (GNX) (12 and 15 mg/kg) or allopregnanolone (ALLO) (15 mg/kg) were administered 15 minutes after status epilepticus (SE) onset and EEG seizure response measured for 5 additional hours. GNX at both dose-levels produced a durable reduction in seizure response (≥ 5 hrs). ALLO produced a shorter duration response (≤ 1 hr).

Id. Saporito P2 concluded "GNX administration elicits a sustained (≥ 5 hrs) block of SE independent of treatment time after SE onset." *Id.*

4. *Marinus Orphan Drug Press Release (Ex. 1011)*

Marinus Orphan Drug teaches "the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation to the intravenous (IV) formulation of its CNS-selective $GABA_A$ modulator, ganaxolone for the treatment of status epilepticus." Ex. 1011, 1.

5. *Marinus Phase I Press Release (Ex. 1022)*

Marinus Phase I Press Release

> announced that it has dosed the first subject in its Phase 1 clinical trial of ganaxolone IV, an intravenous (IV) formulation of Marinus' CNS-selective GABAA modulator, for the treatment of status epilepticus (SE). The study is designed to evaluate the safety, pharmacokinetics (PK) and Pharmacodynamics (PD) of ganaxolone IV in healthy volunteers.

Ex. 1022, 1.

C. Ground 1 – Anticipation over Zhang

1. *Claim 22*

Petitioner asserts

> Zhang teaches a POSA how to make its ganaxolone formulations throughout the specification (including by way of working examples), and also teaches a POSA how to *use* its ganaxolone formulations to treat SE, in particular, by including working examples demonstrating the efficacy of ganaxolone for the treatment of SE in the rat lithium-pilocarpine model.

Pet. 36 (citing Ex. 1009 ¶¶ 116–136; Ex. 1003 ¶ 65) (footnote omitted).

Petitioner asserts

> [e]xample 8 of Zhang describes the effects of ganaxolone in rats with lithium pilocarpine-induced SE.
>
> The rats of Example 8 were administered a CAPTISOL®-ganaxolone formulation intravenously at 12 and 15 mg/kg, administered either 15 or 60 minutes after onset of SE. Therapeutic activity of ganaxolone in the treatment of SE was assessed by determining changes in EEG power for five hours after onset of SE. Ganaxolone at both 12 and 15 mg/kg "produced a very strong reduction in SE amplitude overall."

Pet. 36–37 (citing Ex. 1009 ¶ 117, 118, 134; Ex. 1003 ¶ 66) (footnote omitted). Petitioner specifically asserts, with regard to independent claim 21 from which claim 22 depends, "Zhang teaches that its ganaxolone

formulations 'include parenteral formulations suitable for intravenous infusion,' and teaches a POSA how to use ganaxolone (intravenously) to treat a patient with SE (whether human or rat)." Pet. 44 (citing Ex. 1001, 38:48–51, 40:8–12; Ex. 1003 ¶¶ 89–90) (footnote omitted).

Petitioner asserts, specific to claim 22, that "[w]hile Zhang does not expressly disclose that its ganaxolone formulations provide 'improvement to the patient after administration for more than 8 hours,' this would be the natural result of administering them to a patient with SE, as taught by Zhang. As such, Zhang inherently teaches the limitation of claim 22." Pet. 45 (citing Ex. 1003 ¶ 93).

Petitioner asserts, as a separate basis for Zhang anticipating claim 22, that

> Zhang states: "Methods of treatment also include administering multiple injections of the β-cyclodextrin-ganaxolone injectable formulation over a period of 1 to 10 days. The injections may be given at intervals of 1 to 24 hours." A skilled artisan would immediately recognize that if a single bolus treatment for SE suppresses seizures for up to 2 hours as ganaxolone is clearly shown to do in Tables 6 and 7, then the treatment could be repeated at intervals of 2 hours to provide sustained treatment for more than 8 hours.

Pet. 45 (footnote omitted).

Patent Owner asserts "Petitioner, however, points to nothing in Zhang that describes treating a human patient, let alone one suffering from SE." Prelim. Resp. 32. Patent Owner asserts "[n]or can Petitioner point to any relevant disclosure in Zhang that describes intravenously administering ganaxolone to a human patient suffering from SE. Thus, for this reason alone, Petitioner has not established that Zhang anticipates any of the challenged claims, all of which depend from claim 21." *Id.* Patent Owner

asserts "Petitioner's alleged evidence on this point should be afforded little weight because it is based on attorney argument and supported by conclusory expert testimony that merely repeats the attorney argument near verbatim." *Id.* at 33.

Patent Owner asserts "Petitioner's inherency argument that the 8-hour limitation 'would be the natural result of administering [Zhang's ganaxolone formulations] to a patient with SE' also fails to meet the legal standard." Prelim. Resp. 34. Patent Owner asserts "Petitioner points to no evidence as to why 'improvement to the patient after administration for more than 8 hours' would inevitably happen based on Zhang's disclosure." *Id.* at 35. Patent Owner asserts "Zhang provides no data regarding seizure reduction beyond 5 hours. Zhang therefore cannot inherently anticipate claim 22 because it does not show that the claim limitation inevitably would occur. In fact, it shows the contrary." *Id.* at 35–36.

Patent Owner asserts that "Petitioner's argument that the 8-hour limitation in claim 22 can be satisfied by repeated treatments of ganaxolone 'at intervals of 2 hours' is also without merit for at least three reasons." Prelim. Resp. 36. Patent Owner asserts "[*f*]*irst*, here again, Petitioner improperly relies on what a skilled artisan allegedly would have known to fill the gaps in Zhang." *Id.* Patent Owner asserts "[*s*]*econd*, to draw the conclusion it does from a single general paragraph in Zhang, Petitioner necessarily resorts to improper picking and choosing from different portions of Zhang to allegedly meet this limitation." *Id.* Patent Owner asserts

> *Third*, Zhang's paragraph 74 states only that the β-cyclodextrin ganaxolone "injections may be given at intervals of 1 to 24 hours." Ex. 1009, ¶ [0074]. It does not say anything about treating SE or administering multiple doses of

> ganaxolone to treat any of the at least 31 diseases or disorders identified in Zhang, let alone SE. It also does not state that multiple treatments can prolong an anti-seizure effect from a single treatment such that there is "improvement to the patient after administration for more than 8 hours."

Id. at 38.

We find that, on the current record, the evidence better supports Petitioner's position. Zhang defines a patient as "a human or non-human animal in need of medical treatment." Ex. 1009, 5 ¶ 22. Zhang teaches "Seizure disorders that may be treated with the substituted β-cyclodextrin-ganaxolone injectable formulation include status epilepticus." *Id.*, 13 ¶ 70. Zhang teaches embodiments where the "substituted β-cyclodextrin-ganaxolone injectable formulation is administered as an intravenous infusion dose." *Id.*, 14 ¶ 76.

Thus, contrary to Patent Owner's assertions, Zhang teaches intravenous treatment using a ganaxolone formulation in human patients with status epilepticus. *See, e.g.*, Ex. 1009, 5 ¶ 22, 13 ¶ 70, 14 ¶ 76.

As to the issue of whether it is more likely than not that Zhang inherently satisfies the requirement for "improvement to the patient after administration for more than 8 hours" recited in claim 22, we appreciate that Zhang's working example in rats terminates at 5 hours as the rats are then sacrificed for analysis. Ex. 1009, 24 ¶ 127. Zhang states that in the experiment on rats with induced status epilepticus, ganaxolone "reduced EEG power across all frequency ranges to levels at or below baseline for at up to 5 [hours]." Ex. 1009, 25 ¶ 135. This is the only direct evidence in Zhang and suggests that ganaxolone continued providing improvement up to the 5 hour point. Petitioner's expert states "[t]o the extent that improvement

to the patient were to occur after that time period, however, it would be the natural result of administering the ganaxolone formulations in the manner taught in Zhang." Ex. 1003 ¶ 93.

We appreciate Patent Owner's point that for a reference to anticipate without disclosing the relevant feature of the claimed invention, it is required that the "missing characteristic is necessarily present . . . in the single anticipating reference." *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003). In this case, Zhang demonstrates that ganaxolone continues to improve status epilepticus in rats for 5+ hours, supporting the inherency position. Moreover, the '817 patent's Specification shows that 10 and 20 mg/kg ganaxolone doses that bracket the 12 and 15 mg/kg ganaxolone doses tested by Zhang, result in improved 24-hour survival relative to lower doses. *See* Ex. 1001, Fig. 4; Ex. 1009, 21 ¶ 117. This evidence further supports Petitioner's inherency position because it shows that doses bracketing those recited in Zhang provide continued improvement to patients for periods exceeding 8 hours. "Extrinsic evidence can be used to demonstrate what is 'necessarily present' in a prior art embodiment even if the extrinsic evidence is not itself prior art." *Hospira, Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1329 (Fed. Cir. 2020).

As to the issue of whether Zhang's teaching to treat with multiple doses also teaches "improvement to the patient after administration for more than 8 hours" as required by claim 22, on this record we find that Petitioner's position is more persuasive. Claim 22 does not distinguish between a single administration event or multiple administrations, and therefore is reasonably interpreted as broadly open to both single administration and multiple administrations. This understanding is consistent

with the '817 patent, which teaches that "[g]anaxolone or a pharmaceutically acceptable salt thereof can be administered, e.g., once daily, twice daily, three times daily, or four times daily." Ex. 1001, 8:35–37. Zhang teaches "[d]osing schedules in which the substituted β-cyclodextrin-ganaxolone injectable formulation is injected every 1 hr, 2 hrs, 4 hrs, 6 hrs, 8 hrs, 12 hrs, or 24 hours are included herein." Ex. 1009, 13 ¶ 74. We agree with Petitioner that, on this record, Zhang directly demonstrates that where doses are administered every 1, 2, or 4 hours, the ganaxolone would have been expected to necessarily result in improvement in status epilepticus treatment over more than 8 hours based on the five hour efficacy results reported in Zhang. *See* Ex. 1009, 25 ¶ 135.[9]

We note that either party may submit evidence showing the period of time for which standard doses of ganaxolone necessarily remain effective to improve patients in order to support or rebut the inherency determination, in order to improve the evidentiary record for a final written decision.

Accordingly, Petitioner has demonstrated, on this record, that it will more likely than not prevail on its assertion that claim 22 is unpatentable as anticipated by Zhang.

2. *Claims 25–31*

Petitioner asserts "Zhang discloses 'embodiments in which multiple bolus doses of the ganaxolone/sulfobutyl ether-β-cyclodextrin formulation are administered to the patient.'" Pet. 46–47 (citing Ex. 1009 ¶ 85; Ex. 1003

[9] We note that either party may submit evidence showing the period of time for which standard doses of ganaxolone necessarily remain effective to improve patients in order to support or rebut the inherency determination, in order to improve the evidentiary record for a final written decision.

¶ 102). Petitioner asserts that in "certain embodiments the multiple bolus doses are given over 1 to 10 days at intervals of 1 to 24 hours" and that "[i]n certain embodiments each bolus dose comprises about 1 mg/kg to about 20 mg/kg ganaxolone." *Id.*

Petitioner's expert prepared a table correlating the dose ranges recited in claims 25–31 with the same dose range recited in amounts administered to a 70 kg patient in mg/kg and found that "Zhang's bolus doses of 1 mg/kg to 20 mg/kg, for a 70 kg patient, encompass each of the amounts recited in claims 24–31." Pet. 48 (citing Ex. 1003 ¶ 104).

Patent Owner asserts

> [n]othing in Zhang ties its disclosure of bolus doses of "about 1 mg/kg to about 20 mg/kg" to any one disease state, let alone treating SE. . . . Zhang's general disclosure is not specific to any one disease state, dosage strength, or dosing regimen. Indeed, Zhang includes numerous options beyond dose amount—it also postulates that the ganaxolone formulations could be used to treat at least 31 different diseases or disorders.

Prelim. Resp. 40. Patent Owner contends Zhang "provides several broad dose ranges for administering a ganaxolone formulation in the abstract, and not for any specific disease. . . . This level of picking and choosing from disparate paragraphs in Zhang cannot support Petitioner's anticipation challenge." *Id.* at 41.

We find, on this record, Petitioner's argument is more persuasive regarding anticipation over Zhang. *Ineos* explains that "[i]f the prior art discloses its own range, rather than a specific point, then the prior art is only anticipatory if it describes the claimed range with sufficient specificity such that a reasonable fact finder could conclude that there is no reasonable difference in how the invention operates over the ranges." *Ineos USA LLC v.*

Berry Plastics Corp., 783 F.3d 865, 869 (Fed. Cir. 2015). In this case, there is no dispute that Zhang teaches a range of doses of about 1 mg/kg to about 20 mg/kg of ganaxolone that overlap with the recitation of ganaxolone ranges recited in claims 25–31. *See* Ex. 1009, 15 ¶ 84; Ex. 1003 ¶ 103.

Patent Owner provides no evidence to challenge Dr. Rogawski's statement that "Zhang's bolus doses of 1 mg/kg to 20 mg/kg, for a 70 kg patient, encompass each of the amounts recited in claims 24–31. Therefore, in my opinion, Zhang anticipates claims 24–31." Ex. 1003 ¶¶ 104–105. Petitioner has therefore provided evidence supporting a reason to believe that the doses recited in claims 25–31 would result in no difference in how the claimed subject matter operates, and in particular, that any dose of ganaxolone would function to treat status epilepticus patients and result in improvement to the patient as required by claims 25–31. We note these claims depend from claim 21 and therefore do not recite the "more than 8 hours" language found in claim 22.

Accordingly, Petitioner has demonstrated, on this record, that it will more likely than not prevail on its assertion that claims 25–31 are unpatentable as anticipated by Zhang.

D. Ground 2 – Obviousness over Zhang

1. *Claim 22*

Petitioner asserts

> If Zhang's teachings, as described in Section VIII.A, do not teach the limitations of claim 1–3, 10–17, and 19–31, they suggest them. And, based on Zhang's teachings, including, for example, the results described in Example 8, a POSA would have had a reasonable expectation of success at arriving at the

> claimed methods of treating SE with ganaxolone—whether in a rat patient or a human patient.

Pet. 49 (footnote omitted).

Patent Owner asserts "nowhere does Zhang disclose 'improvement to the patient after administration for more than 8 hours.' Neither the Petition nor Dr. Rogawski's declaration makes any attempt to demonstrate why a skilled artisan would have been motivated by Zhang to arrive at this limitation." Prelim. Resp. 54. Patent Owner further asserts "Petitioner fails to show that a skilled artisan would have had a reasonable expectation of success in using intravenous administration of ganaxolone to achieve an 'improvement to the patient after administration for more than 8 hours.'" *Id.* at 56. Patent owner notes "Zhang provides no data regarding seizure reduction beyond 5 hours." *Id.* at 57.

Patent Owner also asserts "Petitioner fails to show that a skilled artisan would have had a reasonable expectation of success that ganaxolone treatment 'repeated at intervals of 2 hours' would result in 'improvement to the patient after administration for more than 8 hours.'" Prelim. Resp. 58. Patent Owner asserts "Petitioner relies on no evidence demonstrating why a skilled artisan would have had a reasonable expectation of success that multiple, repeated treatments would result in 'improvement to the patient after administration for more than 8 hours' if a single treatment for SE suppresses seizures for up to 2 hours." *Id.*

Patent Owner also asserts objective indicia in favor of patentability, specifically asserting that the "methods of treating SE by administering ganaxolone recited in claims 22 and 25-31 were found to be unexpected and

critical to the claimed invention." Prelim. Resp. 43. Patent Owner cites a Declaration submitted in an application of Petitioner that stated

> Marinus Pharmaceuticals Inc. is investigating the use of ganaxolone for treating SE. Given the complexities of SE and difficulties in treating SE, we initially believed that a *high ganaxolone exposure for a long treatment period of at least 4 days duration, would be required to break SE*, *i.e.*, stop seizures and prevent seizures from rapidly returning when ganaxolone was discontinued.

Prelim. Resp. 45, *citing* Ex. 2007, 30 ¶ 7 (emphasis added by Patent Owner). Patent Owner also points to a phase 2 clinical trial of Petitioner and asserts that the study observed

> "rapid" seizure cessation and reduction in seizure burden and lack of recurrence of SE after discontinuation of the ganaxolone infusion resulting from IV administration of 500 mg/day, 650 mg/day, and 713 mg/day were unexpected over Petitioner's and its scientist's (a person of ordinary skill) expectation that "high ganaxolone exposure for a long treatment period of at least 4 days duration, would be required to break SE."

Prelim. Resp. 47, *citing* Ex. 2007, 30 ¶ 7; Ex. 2008, 26 ¶ 7. Patent Owner asserts

> Petitioner provided that only a dose of 713 mg/day allows for a plasma concentration ≥500 ng/mL for greater than 8 hours and sustained seizure reduction throughout the entire time period tested. As a dose of 713 mg/day falls squarely within the claimed range of 700 mg to 725 mg/day, these statements further confirm that the effects of the 713 mg/day dose on seizure burden reduction and cessation were unexpected over Petitioner's and its skilled artisan scientist's expectations and were markedly superior over the other doses encompassed by Zhang's extremely broad disclosure.

Prelim. Resp. 51.

Patent Owner also asserts the objective indicia of long-felt need and failure of others. Patent Owner asserts the "prior art is replete with statements recognizing the long-felt need for a drug that could treat SE. . . . Ganaxolone administered according to the methods in claims 22 and 25-31 filled this unmet need." Prelim. Resp. 52–53. Patent Owner asserts their

> claimed methods stand against a stark backdrop of repeated failures for treating SE. Intravenous benzodiazepines, such as lorazepam and diazepam, are among the "first-line therapies" for treating SE, but as Petitioner admits, "[a] significant drawback to these therapies is that their efficacy decreases dramatically as the duration of SE increases, and there can be a complete loss of efficacy after a certain amount of time."

Prelim. Resp. 53.

We find that, on this record, Petitioner's reasoning and evidence is more persuasive regarding obviousness over Zhang. As already discussed, Zhang teaches intravenous treatment using a ganaxolone formulation in human patients with status epilepticus. *See, e.g.*, Ex. 1009, 5 ¶ 22, 13 ¶ 70, 14 ¶ 76. And we have already discussed that Petitioner met its institution burden in showing, more likely than not, that Zhang's treatment necessarily results in improvement in the patient for more than 8 hours as discussed above, whether inherently as the ganaxolone formulation remains in effect or through repeated administration every two hours. *See* Ex. 1009, 25 ¶ 135; Ex. 1003 ¶ 93; Ex. 1009, 13 ¶ 74. That is, we think Dr. Rogawski reasonably testifies that a "skilled artisan would immediately recognize that if a single bolus treatment for SE suppresses seizures for up to 2 hours as ganaxolone is clearly shown to do in Tables 6 and 7, then the treatment could be repeated at intervals of 2 hours to provide sustained treatment for more than 8 hours." Ex. 1003 ¶ 94.

Dr. Rogawski's statement supports a finding that a reasonable expectation of success in using ganaxolone for treating a patient with status epilepticus for a period of 8 or more hours. "'[A] reasonable expectation of success, not absolute predictability' supports a conclusion of obviousness." *Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000).

While we agree with Patent Owner that the recited objective indicia support a finding that IV administration of 500 mg/day, 650 mg/day, and 713 mg/day of ganaxolone as sufficient to result in rapid seizure suppression appears to have been unexpected, claim 22 encompasses administration of any dose and therefore is not commensurate in scope with the recited results. Unexpected results must be "commensurate in scope with the degree of protection sought by the claimed subject matter." *In re Harris*, 409 F.3d 1339, 1344 (Fed. Cir. 2005). Nor does Patent Owner provide any nexus between these results and the recited limitation in claim 22 of "improvement to the patient after administration for more than 8 hours."

As to the indicia of long felt need, to establish a long-felt need, three elements must be proven: First, the need must have been a persistent one that was recognized by ordinarily skilled artisans. *In re Gershon*, 372 F.2d 535, 538 (CCPA 1967). Second, the long-felt need must not have been satisfied by another before the invention. *See Newell Companies, Inc. v. Kenney Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988) ("[O]nce another supplied the key element, there was no long-felt need or, indeed, a problem to be solved . . . ."). Third, the invention must, in fact, satisfy the long-felt need. *In re Cavanagh*, 436 F.2d 491, 496 (CCPA 1971).

Even if we agree that there was a long felt need and that Patent Owner's invention satisfies that need, based on the preliminary record, it appears that another, specifically Zhang, already satisfied the need before Patent Owner's invention.

Similarly, we do not find Patent Owner's reliance on the objective indicia of failure by others persuasive as there is no evidence that Zhang, a prior art reference, failed. Thus, rather than show failure by others, the evidence of record suggests success by others.

Accordingly, Petitioner has demonstrated, on this record, that it will more likely than not prevail on its assertion that claim 22 is unpatentable as obvious over Zhang.

2. *Claims 25–31*

Petitioner does not provide separate assertions for these claims but relies upon the same reasoning as recited above.

Patent Owner asserts "Petitioner has failed to demonstrate that a skilled artisan would have been motivated to choose the narrow dose ranges for treating SE recited in claims 25-31 from the broad dose range relied upon by Petitioner in paragraph 85 of Zhang (i.e., 'about 1 mg/kg to about 20 mg/kg ganaxolone')." Prelim. Resp. 59. Patent Owner also asserts "Petitioner fails to show that a skilled artisan would have had a reasonable expectation of success in treating SE with the dose ranges recited in claims 25-31 based on the disclosure of Zhang." Prelim. Resp. 60.

We find claims 25–31 stand on different ground in the obviousness challenge over Zhang because the objective indicia of unexpected results is, based on the preliminary record, reasonably understood to be commensurate in scope with these claims. That is, these claims recite IV administration of

various ranges of ganaxolone per day including ranges of 500 mg to 1000 mg, 625 mg to 650 mg, 650 mg to 675 mg, 675 mg to 700 mg, 675 mg to 700 mg, 625 mg to 700 mg, 700 mg to 725 mg and 1025 mg to 1050 mg. The results cited by Patent Owner show IV administration of 500 mg/day, 650 mg/day, and 713 mg/day of ganaxolone resulted in unexpectedly rapid seizure suppression in status epilepticus. *See* Prelim. Resp. 46, *citing* Ex. 2007, 30 ¶ 7; Ex. 2008, 26 ¶ 7. The other objective indicia of long felt need and failure by others remain unpersuasive for the reasons given above.

As we balance the objective indicia of unexpected results with Petitioner's obviousness position, we question whether Petitioner will likely prevail on this ground with respect to claims 25–31. Notwithstanding the above, our questions will be best resolved on a full trial record.

E. Ground 3 – Obviousness over Zhang, Saporito P1, Saporito P2

1. *Claim 22*

Petitioner asserts "Zhang is described above." Pet. 50. Petitioner asserts that Saporito P1 teaches

> rats were administered lithium chloride (127 mg/kg) and pilocarpine (50 mg/kg) to induce convulsive SE (CSE), a type of SE in which the seizures experienced by the subject are convulsions. Rats were then administered ganaxolone (formulated at a concentration of 2.5 mg/mL in 30% CAPTISOL®) at a dose of 6, 9, or 12 mg/kg at the time of seizure onset (time zero) and 15, 30, and 60 minutes after seizure onset.

Pet. 50, citing Ex. 1013; Ex. 1003 ¶ 112. Petitioner asserts "IV administered ganaxolone 'halted CSE and produced a dose-dependent reduction in seizures associated with CSE when administered at 3 different doses over four separate time points.'" Pet. 50–51, citing Ex. 1013; Ex. 1003 ¶ 113.

Petitioner asserts that Saporito P2 performs a similar experiment on rats to induce SE and showed "the administration of ganaxolone treated SE, by terminating or stopping SE." Pet. 53, citing Ex. 1014, Ex. 1003 ¶ 118.

Petitioner specifically points out, pertinent to claim 22, that the Saporito P1 "poster also shows that the IV administered ganaxolone promotes survival, measured 24 hours after the onset of CSE." Pet. 51, 56 (citing Ex. 1013 at Fig. 3). Petitioner relies on the same reasoning for claims 25–31. *See* Pet. 57.

Patent Owner asserts that "Petitioner has failed to establish that Saporito P1 and Saporito P2 were sufficiently publicly accessible before the priority date of the '817 patent. Saporito P1 and Saporito P2 are not dated, and there is no indication on their face that they were presented at the 2016 AAN meeting." Prelim. Resp. 63. Patent Owner also asserts the "Saporito Declaration does not indicate how many people attended the poster sessions other than the sessions being 'well attended' (Ex. 1015, ¶¶ 10, 21) or that the declarant 'interacted with a number of meeting attendees' at Poster Session IV (*id.*, ¶ 15)." *Id.*

Patent Owner asserts that "Saporito P1 and Saporito P2 also do not disclose intravenously administering to a human patient a pharmaceutical composition comprising ganaxolone or a pharmaceutically acceptable salt thereof." Prelim. Resp. 65. Patent Owner also asserts "Petitioner has provided no motivation to combine different aspects of Zhang to arrive at the limitations recited in claim 22 (i.e., 'improvement to the patient after administration for more than 8 hours')." Prelim. Resp. 66. Patent Owner asserts "Petitioner further fails to show that a skilled artisan would have had a reasonable expectation of success in combining Zhang with Saporito P1

and/or Saporito P2 to arrive at the intravenous administration of ganaxolone resulting in 'improvement to the patient after administration for more than 8 hours.'" Prelim. Resp. 67. Patent Owner asserts "Dr. Rogawski does not opine, and Saporito P1 does not disclose, that increased survival measured 24 hours after the onset of CSE represents an improvement in treating SE after 8 hours." Prelim. Resp. 68.

We first address the issue of whether the Saporito posters are printed publications. *Medtronic* explained that in *Klopfenstein*, a poster of slides was displayed at a professional conference but not distributed to the public and stated

> Under such a scenario, we identified the relevant factors to include: (1) "the length of time the display was exhibited," (2) "the expertise of the target audience" (to determine how easily those who viewed the material could retain the information), (3) "the existence (or lack thereof) of reasonable expectations that the material displayed would not be copied," and (4) "the simplicity or ease with which the material displayed could have been copied.". . . After reviewing these factors, we determined that the reference was sufficiently publicly accessible to count as a "printed publication" for the purposes of § 102(b).

Medtronic, Inc. v. Barry, 891 F.3d 1368, 138182 (Fed. Cir. 2018) (citing *In re Klopfenstein*, 380 F.3d 1345, 1347–50 (Fed. Cir. 2004)).

Petitioner has provided unrebutted evidence that the public was on notice regarding the presentation of the Saporito posters, where the AAN 2016 meeting program listed the Saporito posters as available with presenters standing by the posters. Ex. 1012, 48, 99. Petitioner also submitted a Declaration by Dr. Saporito regarding the Saporito Poster 1 that (1) the "Poster Session II was held from 8:30am to 5:50pm on the 17th, with presenters, including myself, standing by the posters from 4pm to 5:30pm to

interact with the Annual Meeting attendees who chose to stop and view the poster." Dr. Saporito similarly explained that Saporito Poster 2 was also presented during a poster session at the meeting. Ex. 1015 ¶¶ 9, 13. As to the audience expertise, Dr. Saporito stated (2) the AAN Annual Meeting "is attended by both clinicians practicing in neurology and researchers interested in looking for potential new treatments for neurological disorders. I would consider it to be an important and influential gathering in the neurology field." Ex. 1015 ¶ 5. Dr. Saporito stated (3) "[a]s with Saporito Poster 1, because Saporito Poster 2 was shown and presented at the meeting, I understood that the information on the poster would no longer be considered confidential." Ex. 1015 ¶ 13. Dr. Saporito stated (4) "[j]ust as they did for Saporito Poster 1 from Poster Session II, I recall that attendees took notes and photographs while looking at Saporito Poster 2." Ex. 1015 ¶ 15.

We find that the current evidence of record, and in particular the Saporito Declaration, supports a determination that the Saporito posters were publicly available as they were presented at the AAN annual meeting, that these were exhibited to an expert audience for a sufficient time to assimilate or copy the information, and that the poster presenters expected copying of their posters, and that actual photographs of the presentation occurred. Ex. 1015 ¶¶ 5–18.

We find that, on this record, Petitioner's reasoning and evidence is more persuasive regarding obviousness over Zhang, Saporito P1, and Saporito P2. As already noted, Zhang teaches intravenous treatment using a ganaxolone formulation in human patients with status epilepticus. *See, e.g.*, Ex. 1009, 5 ¶ 22, 13 ¶ 70, 14 ¶ 76.

As to the limitation in claim 22 that ganaxolone administration results in improvement in the patient for more than 8 hours, Saporito P1 shows that the number of animals surviving after 24 hours increased after three different ganaxolone doses relative to untreated animals, providing some evidence of improvement in the condition of the animals for more than 8 hours. Ex. 1013, Figure 3. Saporito P2 provides more direct evidence that ganaxolone results in continued treatment of status epilepticus in the animal patients at a 6 hour timepoint as ganaxolone "at both dose-levels produced a durable reduction in seizure response (≥ 5 hrs)." Ex. 1014, Figure 4.

We have considered Patent Owner's assertion that Saporito P1 and Saporito P2 did not study human patients but find it unpersuasive of nonobviousness because animal models are routinely used in medical research and the ordinary artisan, informed by Zhang that ganaxolone would have been useful in treatment of status epilepticus in humans, would have reasonably studied the treatment in animals to determine dosing and timing parameters. "[T]hose of skill in the art understood on the priority date of the '817 patent, and still understand, the rat lithium-pilocarpine model to be a widely accepted model to identify potential treatments for SE. Halting behavioral SE in the model indicates that a test substance is effective in treating the SE condition." Ex. 1003 ¶ 115.

We have considered Patent Owner's assertion regarding a reasonable expectation of success and find that, on this record, efficacy of ganaxolone in the rat pilocarpine model system provides a reasonable expectation of success for use of the treatment in other patients including humans for the same periods of time of treatment. The Saporito posters provide additional evidence supporting a finding that ganaxolone administration would have

reasonably improved patient outcomes for periods of 8 or more hours. Ex. 1013, Figure 3; Ex. 1014, Figure 4. "Obviousness does not require absolute predictability of success … all that is required is a reasonable expectation of success." *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009) (emphasis omitted).

Accordingly, Petitioner has demonstrated, on this record, that it will more likely than not prevail on its assertion that claim 22 is unpatentable as obvious over Zhang, Saporito P1, and Saporito P2.

2. *Claims 25–31*

Petitioner asserts a "POSA would have combined Zhang's teachings (e.g., as described in Section VIII.A.8) with Saporito P1 and/or P2's teachings, as described above. And, for at least the reasons described in Section VIII.B, it would have been with a reasonable expectation of success. Therefore, claims 24-31 would have been obvious." Pet. 57 (footnote omitted).

Patent Owner asserts

> Petitioner has failed to establish that a skilled artisan would have been motivated to choose the narrower dose ranges recited in claims 25-31 from the broader dose range disclosed in Zhang (1 mg/kg to 20 mg/kg). Neither the Petition nor Dr. Rogawski's declaration contends that either of Saporito P1 or Saporito P2 would cure the deficiency in Zhang by providing a motivation for choosing the dose ranges recited in claims 25-31.

Prelim. Resp. 69. Patent Owner also asserts "Petitioner has not shown that a skilled artisan would have had a reasonable expectation of success in treating a human patient suffering from SE with the doses recited in claims 25-31 based on Zhang's disclosure." *Id.* at 70.

As we balance the objective indicia of unexpected results with Petitioner's obviousness position (*see* Prelim. Resp. 41–51), we find the evidence currently of record better supports a finding that claims 25–31 are nonobvious.

Accordingly, Petitioner has not demonstrated, on this record, that it is more likely than not to prevail on its assertion that claims 25–31 are unpatentable as obvious over Zhang, Saporito P1 and Saporito P2.

F. Ground 4 – Obviousness over Zhang, Marinus Orphan Drug Press Release, Marinus Phase I Press Release

1. *Claim 22*

Petitioner asserts "Zhang . . . is described above." Pet. 57. Petitioner asserts that Marinus's Orphan Drug Press Release teaches

> "the U.S. Food and Drug Administration (FDA) granted Orphan Drug Designation to the intravenous (IV) formulation of its CNS-selective $GABA_A$ modulator, ganaxolone, for the treatment of [SE]." It also discloses that "[a] Phase 1 clinical trial evaluating the safety, tolerability and pharmacokinetics of ganaxolone IV is expected to initiate in the
>
> first half of 2016.

Pet. 58, citing Ex. 1011; Ex. 1003 ¶ 125. Petitioner asserts the Marinus's Phase I Press Release teaches the company had "'dosed the first subject in its Phase 1 clinical trial of ganaxolone IV, an intravenous (IV) formulation' for the treatment of SE.'" Pet. 58 (citing Ex. 1022; Ex. 1003 ¶ 126). Petitioner asserts that Marinus's Phase I Press Release "also discloses that the study would 'include a dose escalation of a bolus dosage of ganaxolone IV and a bolus dose of ganaxolone IV, followed by a continuous infusion.'" *Id.* (footnote omitted). Petitioner asserts that for "at least the same reasons set forth for claim 1 . . . claim 22 would have been obvious over Zhang and

Marinus's Orphan Drug Press Release and/or Marinus's Phase I Press Release." Pet. 63–64 (footnote omitted).

Patent Owner asserts "Petitioner makes no effort to establish that a skilled artisan would have been motivated to combine Zhang with Marinus's Orphan Drug Press Release and/or Marinus's Phase I Press Releases to arrive at the limitations recited in claims 22 and 25-31." Prelim. Resp. 70. Patent Owner asserts

> Zhang does not provide a reasonable expectation of success for claims 22 and 25-31. Moreover, Marinus's Orphan Drug Press Release and Marinus's Phase I Press Releases do not cure the deficiencies of Zhang by providing a reasonable expectation that ganaxolone would either (1) successfully provide "improvement to the patient after administration for more than 8 hours," as recited in claim 22

Prelim. Resp. 71.

We find that, on this record, Petitioner's reasoning and evidence is more persuasive regarding obviousness over Zhang, Marinus Orphan Drug Press Release, and the Marinus Phase I Press Release. As already discussed, Zhang teaches intravenous treatment using a ganaxolone formulation in human patients with status epilepticus. *See, e.g.*, Ex. 1009, 5 ¶ 22, 13 ¶ 70, 14 ¶ 76. And we have already discussed we find it likely that Zhang's treatment necessarily results in improvement in the patient for more than 8 hours as discussed above, whether inherently as the ganaxolone formulation remains in effect or through repeated administration every two hours as supported by the Rogawski Declaration. *See* Ex. 1009, 25 ¶ 135; Ex. 1003 ¶ 93; Ex. 1009, 13 ¶ 74.

The Marinus Orphan Drug Press Release and the Marinus Phase I Press Release provide some evidence supporting administration of

intravenous ganaxolone to human patients for treatment of status epilepticus. Ex. 1011, 1; Ex. 1022, 1. Neither reference directly addresses the concerns of claim 22 regarding improvement for at least 8 hours in a patient and therefore do not alter the analysis regarding that limitation.

Accordingly, Petitioner has demonstrated, on this record, that it will more likely than not prevail on its assertion that claim 22 is unpatentable as obvious over Zhang, Marinus Orphan Drug Press Release, and the Marinus Phase I Press Release.

2. *Claims 25–31*

Petitioner asserts

> [f]or at least the same reasons set forth for claim 1, a POSA would have combined Zhang's teachings (e.g., as described in Section VIII.A.8) with the teachings of Marinus's Orphan Drug and Phase I Press Releases, as described above. And, for at least the reasons described in Section VIII.B, it would have been with a reasonable expectation of success. Therefore, claims 24–31 would have been obvious over Zhang and Marinus's Orphan Drug Press Release and/or Marinus's Phase I Press Release.

Pet. 64–65. (footnote omitted).

Patent Owner asserts

> Petitioner fails to show that a skilled artisan would have had a reasonable expectation of success that intravenous . . . administration of ganaxolone at the doses recited in claims 25-31 would treat SE in human patients based on Zhang in combination with Marinus's Orphan Drug Press Release and/or Marinus's Phase I Press Release.

Prelim. Resp. 71. Patent Owner asserts "both Press Releases predate phase 1 clinical trials for testing the safety, tolerability, and pharmacokinetics of

ganaxolone IV—notably, not its efficacy in treating SE—from completing, let alone receiving any reportable data." Prelim. Resp. 72.

As we balance the objective indicia of unexpected results with Petitioner's obviousness position (*see* Prelim. Resp. 41–51), we find the evidence currently of record better supports a finding that Petitioner is not likely to prevail in showing that claims 25–31 are obvious.

Accordingly, Petitioner has not demonstrated, on this record, that it is likely to prevail on its assertion that claims 25–31 are unpatentable as obvious over Zhang, Marinus's Orphan Drug Press Release and, Marinus's Phase I Press Release.

G. Ground 7 – Enablement

Petitioner asserts

> the '817 patent specification contains very little data to support its claims related to treating SE with ganaxolone. If Ovid [Patent Owner] takes the position that the references applied to Challenged Claims 1–3, 10–17, and 19–31, above—which contain as much and, in fact, *more* data to support treating SE with ganaxolone—do not anticipate and/or render them obvious by arguing that the references are not enabling, then the claims of the '817 cannot be enabled.

Pet. 74 (footnote omitted). Petitioner asserts that "[c]laims 21–31 recite a particular dosage form (intravenous), and in some cases, particular concentrations, dosing amounts, or patient outcomes." Pet. 77 (footnote omitted). Petitioner asserts the "'817 patent (unlike Marinus's publications), does not contain any working examples of treating SE (in a rat model or otherwise) using an intravenous dose form." Pet. 77–78 (footnote omitted). Petitioner asserts, regarding doses and patient outcomes, that "a person of skill in the art would certainly not have arrived at them based on the only

dose (20 mg/kg) for which data is presented the '817 patent (Example 3) that could possibly suggest efficacy for treating SE in a rat." Pet. 78 (footnote omitted).

Patent Owner asserts "Petitioner's enablement challenge, however, is facially deficient as it does not address or analyze any of the factors set forth in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988)." Prelim. Resp. 73. Patent Owner asserts

> [i]nstead of providing a cogent analysis grounded in the *Wands* factors, Petitioner makes the conclusory assertion that "a person of skill in the art would certainly not have arrived at [the claimed concentrations, dosing amounts and/or patient outcomes] based on the only dose (20 mg/kg) for which data is presented [in] the '817 patent (Example 3) that could possibly suggest efficacy for treating SE in a rat." Pet., 78 (citing Ex. 1003, ¶¶ 158-160). Dr. Rogawski's declaration fares no better as it merely repeats verbatim the attorney argument in the Petition. *Compare* Pet., 78 *with* Ex. 1003, ¶ 159.

Prelim. Resp. 73–74. Patent Owner asserts "Petitioner's own post-filing date clinical testing, which is grounded in the original disclosure of the '817 patent, shows that the claimed methods of treatment were found to be effective for treating SE, which demonstrates the extent of the '817 patent's enabling disclosure." Prelim. Resp. 74.

While we do not think Patent Owner is correct that caselaw mandates a *Wands* analysis for an enablement analysis as shown by *Amgen Inc. v. Sanofi*, 598 U.S. 594 (2023), which affirmed a non-enablement determination without explicitly addressing any *Wands* factors, we are skeptical on this record that Petitioner is likely to prevail on its enablement challenge, for at least the reasons discussed below.

Claims 22 and 25–31 are narrowly drawn to a particular drug compound, ganaxolone, and a particular disease, status epilepticus. Petitioner provides no evidence that the treatment of status epilepticus patients with ganaxolone was unpredictable, that a large quantity of experimentation was necessary to show ganaxolone efficacy, that the scope of the claim was unduly broad, that the guidance of the '817 specification was insufficient guidance for the claim scope, or that the prior art established concerns regarding the claimed treatment. And while Petitioner does point out that the '817 patent lacks working examples (*see* Pet. 78), we find that, on the current record, the consideration of all of these factors together would tend to support a finding that claims 22 and 25–31 comply with the enablement requirement.

Accordingly, Petitioner has not demonstrated, on this record, that it is likely to prevail on its assertion that claims 22 and 25–31 are unpatentable as failing to comply with the enablement requirement.

III. CONCLUSION

Petitioner has, at this stage, established, more likely than not, that it will prevail in showing that at least one of the challenged claims is unpatentable. This determination is, however, based on a preliminary record and is not final on any issues of patentability. We will make a final determination on the patentability of the challenged claims, as necessary and applying the preponderance of the evidence standard, based on a fully developed record through trial.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 324(a) post grant review of claims 22 and 25–31 of the '817 patent is hereby *instituted* on the grounds set forth in the Petition, commencing on the entry date of this Order, and pursuant to 35 U.S.C. § 324(d) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial.

FURTHER ORDERED that the trial will be conducted in accordance with a separately issued Scheduling Order.

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