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Paper 11
Entered: December 10, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEUROCRINE BIOSCIENCES, INC.,

Petitioner,

v.

SPRUCE BOSCIENCES, INC.,

Patent Owner.

PGR2021-00088
Patent 10,849,908 B2

Before JOHN G. NEW, SUSAN L. C. MITCHELL, and ZHENYU YANG, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner Neurocrine Biosciences, Inc. ("Petitioner") has filed a Petition (Paper 3, "Pet.") seeking post-grant review of claim 1–25 of US Patent 10,849,908 B2 (Ex. 1001, the "'908 patent"). Patent Owner Spruce Biosciences, Inc. ("Patent Owner") timely filed a Preliminary Response. Paper 8 ("Prelim. Resp.").

Under 35 U.S.C. § 324, the Board "may not authorize a post-grant review to be instituted unless … the information presented in the petition … if such information is not rebutted would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." Upon consideration of the Petition, the Preliminary Response, and the evidence presently before us, we determine that Petitioner has failed to demonstrate that it is more likely than not that it would prevail in establishing the unpatentability of at least one challenged claim of the '908 patent. We consequently deny institution of post-grant review.

II. BACKGROUND

A. Real Parties-in-Interest

Petitioner identifies Neurocrine Biosciences, Inc. as the real party-in-interest. Pet. 79. Patent Owner identifies Spruce Biosciences, Inc. as the real party-in-interest. Paper 6, 2.

B. Related Matters

Petitioner states that it is not aware of any disclaimers, reexamination certificates, or petitions for *inter partes* or post grant review for the '908 Patent, nor is Petitioner aware of any pending civil actions involving the

'908 patent. Pet. 80. Patent Owner similarly states that it is not aware of any related matters involving the '908 patent. Paper 6, 2.

C. The Asserted Grounds of Unpatentability

Petitioner contends that claims 1–25 of the '908 patent are unpatentable, based upon the following grounds:

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
I	1–4, 7–9, 11–14, 17–19, 21–24	102	Grigoriadis[1]
II	4, 10, 14, 20–22, 25	103	Grigoriadis
III	5–6, 15–16	103	Grigoriadis, Romano[2]
IV	1–25	112	Lack of written description
V	1–25	112	Lack of enablement

Petitioner also relies upon the Declaration of Dr. Robert M. Carey (the "Carey Declaration," Ex. 1005).

[1] Grigoriadis et al. (US 2017/0020877 A1, January 26, 2017) ("Grigoriadis") Ex. 1006.

[2] Romano (US 2005/0209250 A1, September 22, 2005) ("Romano") Ex. 1007.

D. The '908 Patent

The '908 patent is directed to pharmaceutical compositions comprising -(4-chloro-2-(morpholin-4-yl) thiazol-5-yl)-7-(1-ethylpropyl)-2,5-dimethylpyrazolo (1,5-α) pyrimidine ("Compound 1"), and to methods of using the same for the treatment of congenital adrenal hyperplasia ("CAH"). Ex. 1001, Abstr. Relevantly, the '908 patent is directed to the administration of Compound 1, or another antagonist of the corticotropin releasing factor ("CRF") receptor type 1 ("CRF1"), and thus inhibiting release of adrenal corticotropic hormone ("ACTH") by the secretory cells of the adenohypohysis, for the treatment of CAH. Ex. 1001, cols. 10–12, ll. 47–26.

E. Representative Claims

Independent claims 1 and 11 of the '908 patent recite:

> 1. A method of treating congenital adrenal hyperplasia (CAH) in a human comprising administering to the human a therapeutically-effective amount of a CRF receptor antagonist or a pharmaceutically acceptable salt thereof, wherein an adrenocorticotropic hormone (ACTH) level in the human is reduced by at least 10% from baseline.
>
> 11. A method of treating congenital adrenal hyperplasia in a human comprising administering to the human a therapeutically-effective amount of a CRF receptor antagonist or a pharmaceutically acceptable salt thereof, wherein a 17-hydroxyprogesterone (17-OHP) level is reduced in the human by at least about 10% from baseline.

Ex. 1001 col. 48, ll. 6–42.

F. Prosecution History of the '908 Patent

The '908 patent issued from U.S. Application Ser. No. 16/388,620 (the "'620 application"), filed on April 18, 2019, and claims the priority benefit of, *inter alia*, provisional Application Ser. No. 62/545,406, which was filed on August 14, 2017. Ex. 1001, codes (21–22, 60).

Claims 1–25 of the '908 patent were allowed on September 30, 2020, and the patent issued on December 1, 2020. Ex. 1002, 186; Ex. 1001, code (45). The Petition is consequently eligible for post-grant review. *See 35 U.S.C. § 324*.

III. ANALYSIS

A. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b) (2020). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of

claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

Petitioner proposes constructions for the claim terms "baseline/from baseline," "human," "maintained at a reduced level post 24 hours," and "administered 4 hours prior to sleeping." Pet. 23–28. Patent Owner responds that, of these claim terms, the Board need only construe the claim term "from baseline" for the purposes of institution. Prelim. Resp. 19–20 (citing *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017)).

Having reviewed the pleadings and evidence of record, we conclude that we need only construe the claim term "from baseline" as part of our Decision to deny institution of post-grant review.

1. "from baseline"

Independent claims 1 and 11 recite a reduction of ACTH or 17-OHP by at least 10% "from baseline" after administering a CRF1 receptor antagonist to a CAH patient. *See* Ex. 1001 col. 48, ll. 6–42. Petitioner argues that, based upon the ordinary meaning of the claim language, "baseline" refers to a measurement prior to the administration of a CRF1 receptor antagonist. Pet. 24 (citing Ex. 1005 ¶¶ 36–43). Petitioner observes that the only clinical data in the '908 patent relating to ACTH and 17-OHP describe measuring ACTH and 17-OHP levels "at baseline," i.e. ACTH and 17-OHP levels before the administration of tildacerfont (i.e., Compound 1), a CRF1 receptor antagonist, and ACTH and 17-OHP levels after the administration of the first dose of tildacerfont. *Id.* (citing Ex. 1001 col. 42, ll. 1–16, col. 43, ll. 49–67, Figs. 2–3; Ex. 1005 ¶ 38). Petitioner points to

Figures 2 and 3 of the '908 patent as demonstrating a reduction of ACTH and 17-OHP due to the administration of tildacerfont. *Id.* (citing Ex. 1001, col. 43, ll. 49–67, Figs. 2–3; Ex. 1005 ¶ 39). Petitioner contends that Figures 2 and 3 thus depict the change in ACTH and 17-OHP levels from "baseline," consistent with the ordinary meaning of the term. *Id.*

Petitioner contends that the claims do not require that the measurement be made at any particular point in time. Pet. 24. Therefore, argues Petitioner, the baseline measurement for ACTH and 17-OHP levels may be made at any point in time prior to CRF1 receptor antagonist administration, and then compared to those levels post-CRF1 receptor antagonist administration, measured at the same time of day. *Id.* at 24–25 (citing Ex. 1005 ¶¶ 41–42).

Petitioner also argues that a person of ordinary skill in the art would have understood that "baseline" and "from baseline" allow for glucocorticoid administration during baseline measurements. Pet. 25. Acceding to Petitioner, when studying a new CAH drug like a CRF1 receptor antagonist, a skilled artisan would have allowed the patient to continue his or her usual glucocorticoid treatments during and after baseline measurements to avoid endangering the patient's health. *Id.* (citing Ex. 1005 ¶ 40). Petitioner contends that this is consistent with the clinical example in the '908 patent, which tracked the patients' "background glucocorticoid regimens." *Id.* (citing Ex. 1001 col. 42, ll. 26–32; Ex. 1005 ¶ 40).

Patent Owner urges the Board to construe the claim term "from baseline" at least to the extent necessary to determine whether to reject Petitioner's argument on the merits that the claimed reduction "from baseline" is no different than a reduction relative to a placebo. Prelim. Resp.

11. Patent Owner argues that the prosecution history of the '908 patent is part of the intrinsic evidence of the claims' meaning, if it is in evidence. *Id.* (citing *Phillips*, 415 F.3d at 1317).

Patent Owner notes that Petitioner acknowledges that, during prosecution of the '908 patent, Applicants asserted that ACTH and 17-OHP levels "relative to placebo" as used in Grigoriadis were different from reduction of levels "from baseline." Prelim. Resp. 12 (citing Pet. 19). Petitioner contends that, subsequent to the Final Office Action of November 25, 2019, Applicant submitted a Declaration by Dr. Chris N. Barnes, filed June 15, 2020 (the "Barnes Declaration"). *Id.* (*see* Ex. 1002, 34). In the Barnes Declaration, Dr. Barnes attested that, in the Specification, the hormone levels in the patent "were assessed at baseline, which includes a pre-dose overnight set of serial assessments and a post-dose overnight set of serial assessments following the administration of the first dose at day 1." *Id.* at 12–13 (quoting Ex. 1002, 36–37) (emphasis omitted). Patent Owner contends that Applicants explained that, whereas the prior art reference cited by the Examiner (Grigoriadis) compared ACTH and 17-OHP levels relative to placebo, it failed to demonstrate a reduction by at least 10% from baseline. *Id.* at 13 (citing Ex. 1002, 100).

The Specification expressly teaches that, with respect to the clinical phase 2 trial described in Example 4, "Patients will have overnight [pharmacokinetic/pharmacodynamics] PK/PD assessments performed at baseline, which include an [sic] pre-dose overnight assessment and a post-dose overnight assessment for PK/PD following administration of the first dose." Ex. 1001 col. 42, ll. 12–16. This is the same quotation and clinical trial relied upon by Dr. Barnes in his Declaration, and is the only definition

of a "baseline" in the '908 patent. *See* Ex. 1002, 36–37. We note that placebos were evidently not employed in the phase 2 clinical study of Example 4.[3]

Given the sole exemplary description of "baseline" in Example 4 of the Specification, we construe the claim term reciting "reduced by at least 10% from baseline" as meaning "a reduction of at least 10% in the level of ACTH (claim 1) or 17-OHP (claim 11) compared to measurements of ACTH or 17-OHP made prior to, and/or at the beginning of, administration of the drug."

B. A Person of Ordinary Skill in the Art

Petitioner contends that a person of ordinary skill in the art would typically possess a medical degree or a Ph.D. in a field related to endocrinology, and would have knowledge of hormone regulation and disorders, as well as knowledge of the treatment regimens employed to treat such disorders. Pet. 60 (citing Ex. 1005 ¶ 34). Petitioner argues that such a person of ordinary skill would also have at least three years of experience conducting research concerning endocrine disorders, including CAH or other adrenal disorders. *Id.*

Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Preliminary Response. For the purposes of this Decision, because we find Petitioner's definition to be consistent with the demonstrable level of skill in the art (*see, e.g.*, Exs. 1009, 1025, 2003, 2004,

[3] We note that placebos were to be employed in the yet-to-be-performed phase 3 clinical trial described in Example 7 of the Specification. *See* Ex. 1001 col. 46, ll. 29–34.

2005), and in the absence of a different proposed definition of the level of skill in the art by Patent Owner, we adopt Petitioner's definition.

C. Ground I: Alleged Anticipation of Claims 1–4, 7–9, 11–14, 17–19, 21–24 by Grigoriadis

1. Overview of Grigoriadis

Grigoriadis is directed to methods for treating CAH by administering to a subject in need thereof an effective amount of a CRF1 receptor antagonist, including (but not limited to) bedtime administration. Ex. 1006 ¶ 7. Grigoriadis teaches that CAH is a group of autosomal recessive genetic disorders that result in little or no cortisol biosynthesis. *Id.* at ¶ 4. Grigoriadis teaches that:

> Corticotropin-releasing factor (CRF)[4] activates the CRF_1 receptor, a class B G protein-coupled receptor (GPCR), and that CRF1 receptor antagonists have the potential to directly inhibit ACTH release in patients with CAB, thereby allowing normalization of androgen production while using lower, more physiologic doses of hydrocortisone, and reducing treatment-associated side effects.

Id. at ¶ 6.

Relevantly, Example 6 of Grigoriadis teaches a clinical study, entitled "A Phase 1, Single-Blind, Placebo-Controlled, Fixed-Sequence, Single-Dose Study to Evaluate the Safety and Tolerability of NBI-77860 in Adult Females with Congenital Adrenal Hyperplasia (IND 117, 388)." *Id.* at ¶ 90. The study comprised a single-blind, placebo-controlled, single center, fixed-

[4] The terms "corticotropin releasing factor" (CRF) and "corticotropin releasing hormone" (CRH) as used herein are synonymous.

sequence single-dose clinical trial in adult female classical CAH patients, designed to "assess the safety, tolerability, and plasma exposure of verucerfont (NBI-77860), a CRF1 receptor antagonist, as well as the effect of this compound on endogenous levels of [hypothalamic-pituitary-adrenal] axis hormones." *Id.*

The dosage regiment and experimental design of this study is depicted in Figure 4 of Grigoriadis, which is reproduced below:

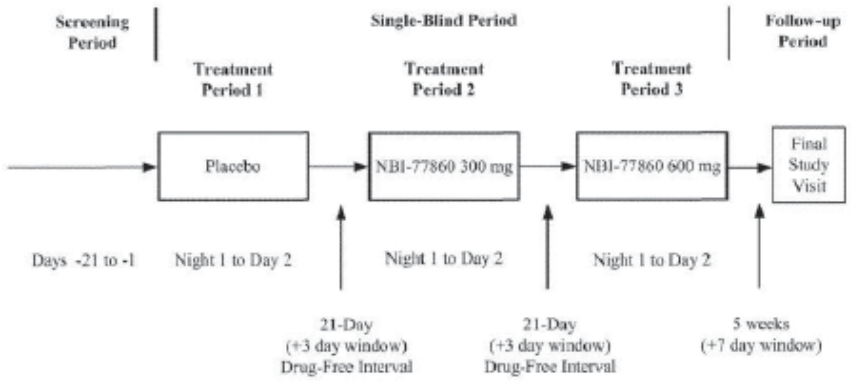

Figure 4 of Grigoriadis depicts the dosage regimen and experimental design of the clinical phase 1 study of Example 6

In the study, a total of eight female subjects, ages 19 to 58, with a medical diagnosis of classical 21-hydroxylase deficiency AH were administered single bedtime doses (hs) of placebo and verucerfont 300 mg, and 600 mg during three separate treatment periods. *Id.* at ¶ 91. The results of the study are depicted in Figure 5 of Grigoriadis, reproduced below:

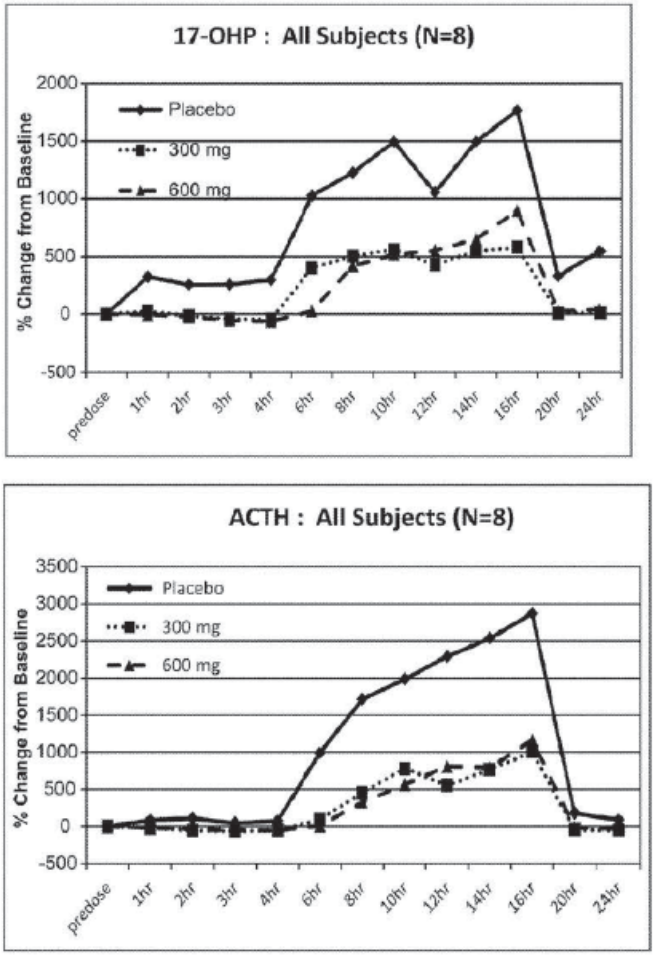

Figure 5 of Grigoriadis depicts levels of 17-OHP and ACTH in response to placebo and 300 mg and 600mg doses of verucerfont during the 24-hour, post-dose periods

Grigoriadis teaches:

Consistent and clinically meaningful reductions from predose levels of both 17-OHP and ACTH were observed throughout the postdose period following administration of NBI-77860 relative to placebo in these CAH patients. In addition to the group mean data, individual responses were evaluated and treatment "responders" were conservatively defined as those subjects with at least a 50% decrease in 17-OHP and ACTH under active NBI-77860 relative to placebo during the peak morning period. This responder analysis yielded a sizeable responder rate of 50% in

> the study (none of these subjects were responders during the initial placebo treatment period). Furthermore, the 300 mg dose yielded nearly identical effects on 17-OHP and ACTH as the 600 mg dose.

Ex. 1006 ¶ 93.

2. Anticipation of Claims 1–4, 7–9, 11–14, 17–19, and 21–24 by Grigoriadis

a. Independent claims 1 and 11

Petitioner argues that Grigoriadis teaches crinecerfont (SSR-125543), a CRF1 receptor antagonist, as useful for the treatment of CAH. Pet. 47 (citing Ex. 1006 ¶ 54). Petitioner contends that Grigoriadis also discloses a range of therapeutically acceptable amounts of a CRF1 receptor antagonist, of about 50–1000 mg. *Id.* (citing Ex. 1006 ¶ 63). According to Petitioner, the administration of a therapeutically effective amount of crinecerfont to a patient, as taught by Grigoriadis necessarily, and thus inherently, results in an at least 10% reduction of the patient's levels of ACTH and 17-OHP, compared to the patient's baseline. *Id.* (citing Ex. 1005 ¶¶ 53–62; Ex. 1009, 10, 13–19, Figs. 1–2, Table 2).

The factual basis of this inherency, argues Petitioner, is demonstrated by R.J. Auchus et al., *Crinecerfont Lowers Elevated Biomarkers of Disease Control in Adults with Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency*, ("Auchus") a manuscript that has been submitted for review for publication in The Lancet. Ex. 1009. According to Petitioner, Auchus teaches a Phase 2 clinical study demonstrating that the administration of crinecerfont to patients with CAH resulted in at least a

10% reduction in ACTH and 17-OHP compared to the patient's baseline levels prior to administration of crinecerfont. Pet. 30 (citing Ex. 1005 ¶¶ 54–62; Ex. 1009, 11, 13–19, Figs. 1–2, Table 2. Petitioner contends that the clinical study tested four dosing regimens, with patients in four cohorts receiving between 50 mg and 200 mg of crinecerfont per day, administered for 14 consecutive days. *Id.* at 30–31 (citing Ex. 1005 ¶ 55; Ex. 1009, 10). Petitioner argues that the Auchus study measured the patients' baseline ACTH and 17-OHP levels over a 24-hour period beginning in the evening of the seventh day before the study began (Day -7 to Day -6). *Id.* at 31 (citing Ex. 1005 ¶ 56; Ex. 1009, 10–11, Fig. 1). After 14 days of repeated dosing of crinecerfont, the patients' ACTH and 17-OHP levels were measured over a 24-hour period beginning in the evening of Day 14 and ending on Day 15. *Id.*

Petitioner asserts that the reduction in ACTH and 17-OHP levels compared to baseline exceeded 10% for patients in all four cohorts after receiving crinecerfont for 14 days. Pet. 31 (citing Ex. 1005 ¶ 57; Ex. 1009, 13–19, Figs. 1–2, Table 2). Petitioner points to Figure 1 of Auchus, which, Petitioner argues, presents 24-hour profiles of median patient ACTH and 17-OHP by cohort, at baseline and at Day 14. *Id.* (citing Ex. 1005 ¶ 58; Ex. 1009, Fig. 1). Petitioner asserts that the results of the Auchus study show that "[t]reatment with crinecerfont for 14 days led to substantial median reductions for ACTH, 17-OHP, and androstenedione relative to baseline, especially during the morning window, across all cohorts (Figure 1)." *Id.* (citing Ex. 1005 ¶ 58; Ex. 1009, 14).

Petitioner asserts that the "morning window" is clinically relevant because the body's natural circadian release of ACTH occurs in the early

morning hours. Pet. 32 (citing Ex. 1005 ¶ 19; Ex. 1006 ¶ 66). According to Petitioner, in the absence of treatment, the highest ACTH and 17-OHP levels in CAH patients are observed in the morning; reducing ACTH and 17-OHP during this time period is an important objective of any CAH treatment. *Id.* (citing Ex. 1005 ¶¶ 19, 59; Ex. 1009, 11).

Petitioner argues further that Auchus also examined median percent reductions in patient ACTH and 17-OHP levels during the clinically relevant morning window (6–10 a.m.) after 14 days of receiving crinecerfont compared to baseline morning window measurements. Pet. 34 (citing Ex. 1005 ¶ 59; Ex. 1009, 11, 14, Fig. 2, Table 2). Petitioner contends that Auchus reports that in all cohorts, median ACTH and 17-OHP "were reduced from baseline to Day 14 whether based on samples collected during the morning window or the 24-hour sampling period. *Id.* (citing Ex. 1009, Supplementary Table 1). Petitioner asserts that the ACTH and 17-OHP, median percent decreases from baseline were generally similar across cohorts, ranging from -53% to -66%. *Id.* (citing Ex. 1005 ¶ 60; Ex. 1009, 14, Fig. 2).

Petitioner also notes that Auchus reports the number of patients with a greater than 50% reduction in ACTH and 17-OHP at Day 14 compared to baseline levels. Pet. 36 (citing Ex. 1005 ¶ 62; Ex. 1009, Table 2). Petitioner argues that Table 2 of Auchus demonstrates that 50% of patients in Cohort 1, 71% of patients in Cohort 2, 63% of patients in Cohort 3, and 75% of patients in Cohort 4 demonstrated a greater than 50% reduction in ACTH at Day 14 compared to the patient's baseline level. *Id.* (citing Ex. 1005 ¶ 62; Ex. 1009, Table 2).

Summarizing, Petitioner asserts that administration of a therapeutically effective amount of crinecerfont to a patient, as taught by Grigoriadis, would necessarily result in an at least 10% reduction in a patient's ACTH level from baseline, and necessarily results in an at least 10% reduction in a patient's ACTH level from baseline, and therefore inherently anticipates claims 1 and 11 of the '908 patent. Pet. 48.

b. Analysis

We are not persuaded that Petitioner has established that it is more likely than not that independent claims 1 and 11 are anticipated by Grigoriadis. "For a claim to be anticipated, each claim element must be disclosed, either expressly or inherently, in a single prior art reference, and the claimed arrangement or combination of those elements must also be disclosed, either expressly or inherently, in that same prior art reference." *Therasense, Inc. v. Becton, Dickinson and Co.*, 593 F.3d 1325, 1332–33 (Fed. Cir. 2010).

The single clinical trial taught by Example 6 of Grigoriadis does not establish a baseline value for patients against which to compare the data obtained from patients receiving 300 mg or 600 mg of the test drug, NBI-77860 (verucerfont). *See* Ex. 1006 ¶¶ 90–94. Specifically, Example 6 does not establish a baseline "which include[s] an [sic] pre-dose overnight assessment and a post-dose overnight assessment for PK/PD following administration of the first dose," as disclosed by the '908 patent. *See* Ex. 1001, col. 42, ll. 12–16. We therefore conclude that Grigoriadis fails to disclose expressly the limitations of claims 1 and 11 severally reciting

"wherein [the] … hormone … level in the human is reduced by *at least 10 % from baseline*."

Petitioner argues that Grigoriadis inherently discloses this limitation. A reference may anticipate if a claim limitation that is not expressly disclosed is inherently disclosed because it "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); *see also Agilent Techs., Inc. v. Affymetrix, Inc.*, 567 F.3d 1366, 1383 (Fed. Cir. 2009) (holding that the "very essence of inherency is that one of ordinary skill in the art would recognize that a reference unavoidably teaches the property in question").

In support of its argument that Grigoriadis inherently teaches the limitation in question, Petitioner points to Auchus. Auchus discloses a phase 2 study that orally administered crinecerfont (NCT03525886/NBI-74788) to a mixed-gender group of 18 patients for 14 consecutive days as follows: 50 or 100 mg once-daily at bedtime (Cohorts 1 and 2, respectively); 100 mg once-daily in the evening (Cohort 3); 100 mg twice-daily (BID, Cohort 4). Ex. 1009, 5. Participants could enroll in more than one cohort. *Id.*

In the Auchus clinical trial, changes from baseline to Day 14 in adrenocorticotropic hormone (ACTH), 17-hydroxyprogesterone (17-OHP), androstenedione, and testosterone were evaluated. Ex. 1009, 5. Auchus further discloses that baseline is established for the participant subjects *via* admitting them to the study center "from Day -7 to -6 [i.e. from day 7 to day 6 *prior* to the initial administration of the drug] for serial blood sampling to establish baseline ACTH, 17-OHP, androstenedione, and testosterone

concentration profiles." *Id.* at 12. Although this method of establishing a baseline is somewhat different than that employed by Grigoriadis, the effect is essentially the same, to establish for each patient the metabolic baseline levels of the concentration of each of the hormones measured, to be compared against the same hormones subsequent to administration of the test drug.

However, the Auchus and Grigoriadis clinical trials vary in several important ways. Most significantly, the two trials employ different CRF1 receptor antagonists: Grigoriadis discloses administration of verucerfont ((NBI-77860), whereas Auchus discloses administration of crinecerfont (NBI-74788/SSR-125543). Ex. 1006 ¶ 90; Ex. 1009, 5. Table 1 of Patent Owner's Preliminary Response, reproduced below, outlines other significant differences between the studies:

Grigoriadis	EX1009
Treatment period: 1 day. EX1006, ¶90, FIG. 4.	Treatment period: 14 days. EX1009, 11.
Study drug: verucerfont (NBI-77860). EX1006, ¶90.	Study drug: crinecerfont (NBI-74788). EX1009, 5; Paper 4, 2.
Placebo administered before study drug. EX1006, ¶90.	No placebo administered before study drug. EX1009, 10-11.
Patients: all female. EX1006, ¶91.	Patients: 11 women, 7 men. EX1009, 5.
Dose size: 300, 600 mg. EX1006, ¶91.	Dose size: 50-100 mg. EX1009, 5.
Dosing regimen: single dose at bedtime. EX1006, ¶91.	Dosing Regimen: 14 consecutive days of single dose or twice daily EX1009, 5.

Prelim. Resp. 32.

Given these differences, and particularly the difference in the study drugs employed in Grigoriadis and Auchus, we cannot agree with Petitioner that the results of the Auchus clinical trial demonstrate that the single clinical trial of a different drug, as disclosed by Grigoriadis, *necessarily* discloses "at least 10% reduction in a patient's ACTH level from baseline, and therefore inherently anticipates claims 1 and 11 of the '908 patent." Pet. 48. A persuasive demonstration of inherency would seem to require a study replicating that of Grigoriadis (and at least employing the identical study drug) and including baseline measurements against which to compare the Grigoriadis results. The Auchus clinical trial, for the reasons we have explained above, does not provide such proof of inherency.

To be sure, Grigoriadis discloses crinecerfont, the study drug employed in the Auchus clinical trial. *See* Ex. 1006 ¶ 54. But Grigoriadis discloses crinecerfont ([4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2 cyclopropyl-1-(3-fluoro-4-methylpbenyl) ethyl]-5-mcthyl-N-(2-propyn-l-yl)-2-thiazolamine) as an example of a CRF1 receptor antagonist. However, crinecerfont is *not* disclosed by Grigoriadis as being a study drug in any clinical trial similar to its Example 6; it is mentioned only as being one of a class of CRF1 receptor antagonists. And although Grigoriadis discloses that crinecerfont is a species of CRF1 receptor antagonist, Petitioner may not attempt to import experimental results from Auchus that are not prior art to the '908 patent in an attempt to show that crinecerfont inherently has clinical properties that were not already demonstrated in Grigoriadis.[5]

[5] We also note that this reasoning was expressly employed by the Examiner during prosecution of the '908 patent, who stated in both the Non-Final Office Action of July 15, 2019 and the Final Office Action of October 4,

Nor is Petitioner's inherency argument commensurate with the scope of the claims. Claims 1 and 11 recite administering to a human "a therapeutically-effective amount of a CRF receptor antagonist or a pharmaceutically acceptable salt thereof." Petitioner's declarant, Dr. Carey, acknowledges that "[b]ased on my review of the published literature, over 100 CRF1 receptor antagonists had been characterized or were in clinical development prior to the filing of the '908 patent, including NBI34041, verucerfont, and pexacerfont. Ex. 1005 ¶ 99 (citing Ex. 1029; Ex. 1018; Ex. 1030; Ex. 1031). Petitioner has not demonstrated that all, or even a representative number of this genus have necessarily demonstrated an "at least 10% reduction in a patient's ACTH level from baseline."

Grigoriadis may well support an obviousness challenge to claims 1 and 11, however Petitioner has not made that argument, or challenged independent claims 1 and 11 as unpatentable under 35 U.S.C. § 103. And because we find that: (1) Grigoriadis does not expressly disclose all of the limitations of claims 1 and 11; and (2) Auchus does not support Petitioner's argument that Grigoriadis inherently discloses the non-expressly taught limitations of claims 1 and 11, we conclude that Petitioner has failed to

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2019, that "The prior art is not anticipatory insofar as these combinations must be selected from various lists/locations in the reference." Ex. 1002, 113, 87. Although we need not reach Patent Owner's arguments with respect to 35 U.S.C. § 325(d), we find this finding of the Examiner to be relevant here, because we agree that the disclosure of crinecerfont as a CRF1 receptor antagonist, but the lack of any clinical showing of crinecerfont's efficacy, demonstrates that Grigoriadis does not anticipate claims 1 and 11.

establish that it is more likely than not that Grigoriadis anticipates claims 1 and 11 of the '908 patent.

c. Dependent claims 2–4, 7–9, 12–14, 17–19, 21–24

Claims 2–4, 7–9, and 21 depend, directly or indirectly, from claim 1. Claims 12–14, 17–19, and 22 depend, directly or indirectly, from claim 11. Claims 23 or 24 depend from either claims 1 or 11. Petitioner makes arguments that these dependent claims are also anticipated by Grigoriadis. *See* Pet. 51–58. However, because we conclude, for the reasons explained *supra*, that Petitioner is not reasonably likely to prevail in proving at trial that Grigoriadis anticipates the independent claims, we similarly conclude that Petitioner has not established a likelihood of similarly prevailing with respect to the dependent claims.

D. Ground II: Obviousness of Claims 4, 10, 14, 20–22, and 25 by Grigoriadis

These claims depend, directly or indirectly, from independent claims 1 or 11. Petitioner argues that, because:

> [A]dministering a CRF1 receptor antagonist at a dose of 200 mg/day is inherently anticipated by Grigoriadis's disclosure of crinecerfont to treat CAH, and Neurocrine's Phase II clinical data reported in Auchus 2021 demonstrating that administration of 200 mg/day crinecerfont results in the claimed ACTH and 17-OHP reductions from baseline. These [dependent] claims are also obvious in view of the disclosure of NBI-77860 in Grigoriadis.

Pet. 61 (citing Ex. 1005 ¶¶ 72–73). In effect, Petitioner argues that these dependent claims are obvious variations of the allegedly anticipated claims 1 and 11. *See id.*

However, as we have explained *supra*, we have concluded that Petitioner has failed to establish that it is more likely than not that independent claims 1 and 11 are anticipated by Grigoriadis. Petitioner makes no argument that independent claims 1 and 11 are obvious over Grigoriadis. Because Petitioner's arguments with respect to Ground II rely in principal part in showing that dependent claims 4, 10, 14, 20–22, and 25 are obvious in view of the alleged anticipation of claims 1 and 11 by Grigoriadis, Petitioner's arguments must again fail. We therefore conclude that Petitioner has failed to establish that it is more likely than not that dependent claims 4, 10, 14, 20–22, and 25 are obvious over Grigoriadis.

E. Ground III: Obviousness of Claims 5–6 and 15–16 by Grigoriadis and Romano

1. Overview of Romano

Romano is directed to:

> [A] pharmaceutical compositions [sic] for treating, for example, mood disorders or conditions, psychotic disorders or conditions, or a combination thereof, in a mammal such as a human, the composition comprising (a) an atypical antipsychotic, a prodrug thereof or a pharmaceutically acceptable salt of the atypical antipsychotic or prodrug thereof, (b) a corticotropin releasing factor antagonist, a prodrug thereof, or pharmaceutically acceptable salt of said corticotropin releasing factor antagonist or prodrug thereof, and optionally (c) a pharmaceutically acceptable vehicle, carrier or diluent.

Ex. 1007, Abstr. Specifically, Romano teaches that "[i]n particular, CRF antagonists have been described as effective in the treatment of, for example, stress-related illnesses; mood disorders such as depression, including, for example, depression in cancer patients, depression in Parkinson's patients." *Id.* at ¶ 10.

With response to its formulations, Romano teaches:

> The pharmaceutical compositions of the present invention can consist of a combination of immediate release and controlled release characteristics. *Such compositions can take the form of combinations of the active ingredients that range in size from nanoparticles to microparticles* or in the form of a plurality of pellets with different release rates. The tablet or capsule composition of the present invention can contain an atypical antipsychotic in sustained or controlled release form and the CRF antagonist in an immediate release form. Alternatively, the atypical antipsychotic can be in immediate release form and the CRF antagonist can be in sustained or controlled release form.

Ex. 1007 ¶ 531 (emphasis added).

2. Alleged obviousness of claims 5–6 and 15–16 over Grigoriadis and Romano

a. Petitioner's contentions

Dependent claim 5 is representative of these claims, and recites "the method of claim 1, wherein said CRF receptor or a pharmaceutically acceptable salt thereof is in the form of microparticles." Ex. 1001 col. 48, ll. 22–26. Claims 6 and 16 further define the size range of the microparticles as being between 1 m and 20 m. *Id.* at col. 48, ll. 27–28, 57–58.

Petitioner acknowledges that Grigoriadis does not explicitly disclose administering the CRF1 receptor antagonist in the form of microparticles. Pet. 68. According to Petitioner, however, it would have been obvious to formulate the CRF1 receptor antagonists disclosed by Grigoriadis as microparticles with an average size of between about 1–20 μm, as taught by Romano. *Id.* Petitioner contends that Romano expressly teaches that the active ingredients of Romano's claimed compositions, a CRF1 receptor antagonist and an atypical antipsychotic, can range in size from nanoparticles to microparticles. *Id.* at 68–69 (citing Ex. 1005 ¶¶ 76–77; Ex. 1007 ¶ 531). According to Petitioner, a person of ordinary skill in the art would have understood Romano as teaching the use of small particle sizes with CRF1 receptor antagonists, such as the claimed range of between about 1–20 μm. *Id.* at 69.

Petitioner argues further that a person of ordinary skill in the art would have been motivated to combine the teachings of Grigoriadis with Romano because both relate to pharmaceutical compositions comprising a CRF1 receptor antagonist. Pet. 69 (citing Ex. 1005 ¶ 77; Ex. 1006 ¶ 61; Ex. 1007 ¶ 531). Furthermore, argues Petitioner, a skilled artisan would have known that microparticles could be used to create sustained release formulations, and would have been motivated to combine Grigoriadis and Romano because both disclose using a CRF1 receptor antagonist in a sustained release formulation. *Id.* (citing Ex. 1005 ¶ 77; Ex. 1006 ¶ 73; Ex. 1007 ¶ 531; Ex. 1023, 2; Ex. 1035, 309–310, 349–350). Petitioner asserts that Grigoriadis teaches that CRF1 receptor antagonist compositions could generally be prepared using well-known technology, and a person of ordinary skill would have been familiar with microparticles as a common

form of administering a pharmaceutical active ingredient. *Id.*, 69–70 (citing Ex. 1005 ¶ 77; Ex. 1006 ¶ 73; Ex. 1023, 2; Ex. 1035, 309–310, 349–350).

b. Analysis

We conclude that Petitioner's argument with respect to Ground III must fail, because, again, Petitioner has made no argument or showing with respect to this Ground, or with respect to Grounds I and II, that any of the limitations of independent claims 1 and 11, from which claims 5–6 and 15–16 depend, and each of which therefore incorporate the limitations of the independent claims, are obvious over Grigoriadis. *See Robotic Vision Sys., Inc. v. View Eng'g, Inc.*, 189 F.3d 1370 1376 (Fed. Cir. 1999) (holding that dependent claims are to be construed to incorporate by reference all of the limitations of the claims from which they depend (citing 35 U.S.C. § 112)). Petitioner advances no ground or basis that the limitations of independent claims 1 and 11 are obvious over Grigoriadis, but argues *only* that these claims are anticipated.

We have explained in Section III.C.2.b, *supra*, why we have concluded that Petitioner has failed to establish that it is more likely than not that independent claims 1 and 11, from which claims 5–6 and 15–16 depend, are anticipated by Grigoriadis. The Petition makes no argument, and adduces no evidence of record, to show that the limitations of the independent claims, which must be construed as being incorporated by reference into claims 5–6 and 15–16, are obvious over Grigoriadis. See *Robotic Vision*, 189 F.3d at 1376. Absent any such argument, Petitioner has failed to demonstrate that it is more likely than not that these dependent claims are obvious over Grigoriadis.

F. Ground IV: Claims 1–25 Lack of Written Descriptive Support

1. Petitioner's Contentions

Petitioner argues that the claims of the '908 patent fail the written description requirement because the '908 patent does not show possession of the claimed subject matter. Pet. 72. Petitioner contends that the claims are broad and recite methods of treating CAH that employ a "CRF1 receptor antagonist or a pharmaceutically acceptable salt thereof" that reduces ACTH or 17-OHP by at least 10% from baseline. *Id.* Petitioner asserts that these are "functionally defined" claims that are unbounded structurally and are limited only by the achieved effect on ACTH and/or 17-OHP. *Id.* Petitioner points to our reviewing court's opinion in *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336 (Fed. Cir. 2010) (en banc), as requiring that the patent must disclose either a representative number of species or common structural features. *Id.* at 72–73 (citing *Ariad*, 598 F.3d 1350).

Petitioner notes that CRF1 receptor antagonists represent a large, structurally diverse class of over 100 compounds, but asserts that the '908 patent discloses only a single CRF1 receptor antagonist, tildacerfont (Compound 1). Pet. 73 (citing Ex. 1005 ¶¶ 98–100). Furthermore, argues Petitioner, all of the Examples and clinical data in the '908 patent relate to tildacerfont. *Id.* (citing Ex. 1001, cols. 34–47, ll. 5–58, Tables 5–8). Petitioner contends that the '908 patent does not disclose the use of any other CRF1 receptor antagonist to treat CAH, or disclose structural features common to the members of the genus so that one of skill in the art could visualize or recognize the members of the genus. *Id.* at 73–74.

2. Patent Owner's Preliminary Response

Patent Owner responds that Petitioner incorrectly assumes there is a *per se* rule that a claim is invalid if there is only one working example in the specification. Prelim. Resp. 39. Patent Owner argues that *Ariad* states no such rule, noting that *Ariad* involved a patent application that disclosed no example of any species actually being used to achieve the claimed result. *Id.* (citing *Ariad*, 598 F.3d at 1356). Patent Owner argues that there is no rule categorically requiring disclosure of using more than one antagonist from a known class to provide written description support for a method directed to using that class, and points to a recent Board decision rejecting the same arguments made by Petitioner. *Id.* (citing *Merck Sharp & Dohme Corp. v. Genentech, Inc.*, PGR2021-00039, Paper 10 at 7, 13–22 (July 24, 2021) (denying institution challenging, *inter alia*, written description of claims to a method for treating cancer by administering a PD antagonist together with a TIGIT antagonist)).

Patent Owner contends that the '908 patent is directed to a method of treatment using a CRF1 receptor antagonist that is exemplified by actual reduction to practice—a working example demonstrating the inventors were in possession of the claimed invention. Prelim. Resp. 41. According to Patent Owner, the Specification of the '908 patent discloses using a CRF1 receptor antagonist, in the manner claimed, to achieve the claimed results. *Id.* Patent Owner points out that Petitioner's declarant acknowledges that a person of ordinary skill in the art would, at the time of filing, have been in possession of a discrete class of approximately 100 CRF1 receptor antagonists that had already "been characterized or were in clinical

development prior to the filing of the '908 patent." *Id.* (quoting Pet. 73; *see also* Ex. 1005 ¶ 99).

Patent Owner therefore distinguishes the present case from *Ariad* because the Specification of the '908 patent discloses an example practicing the invention, and referred to a known class of CRF1 receptor antagonists that would have been recognized by a skilled artisan. *Id.* (citing Pet. 71).

3. Analysis

We conclude that Petitioner has not established that it is more likely than not that any claim in Ground IV is unpatentable upon this Ground. "The essence of the written description requirement is that a patent applicant, as part of the bargain with the public, must describe his or her invention so that the public will know what it is and that he or she has truly made the claimed invention." *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1298 (Fed. Cir. 2014) (citing *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 736 (2002)).

According to our reviewing court:

> [W]e have repeatedly indicated that the written description requirement does not demand either examples or an actual reduction to practice. *Ariad*, 598 F.3d at 1352. What it does demand is that one of skill in the art can "visualize or recognize" the claimed antibodies based on the specification's disclosure. *Eli Lilly*, 119 F.3d at 1568. In other words, the specification must demonstrate constructive possession…. *Ariad*, 598 F.3d at 1352.

Centocor Ortho Biotech, Inc. v. Abbott Laboratories, 636 F.3d 1341, 1353 (2011); *see also, e.g.*, *Abbvie*, 759 F.3d at 1299:

> One particular question regarding the written description requirement has been raised when a genus is claimed but the

> specification only describes a part of that genus that is insufficient to constitute a description of the genus.
> ….
>
> "For generic claims, we have set forth a number of factors for evaluating the adequacy of the disclosure, including 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'"
> …..
>
> Here, the claimed invention is a class of fully human antibodies that are defined by their high affinity and neutralizing activity to human IL–12, a known antigen. AbbVie's expert conceded that the '128 and '485 patents do not disclose structural features common to the members of the claimed genus. The question therefore is whether the patents sufficiently otherwise describe representative species to support the entire genus.

(Internal references and citations omitted).

The challenged claims recite a genus ("a CRF1 receptor antagonist or pharmaceutically acceptable salt thereof) that is not itself claimed. The claims, rather, are directed to a method of using that genus in the treatment of CAH. The prior art cited by Petitioner acknowledges that the genus of CRF1 receptor antagonists was well known in the art at the time of invention. *See* Ex. 1006, *e.g.*, ¶¶ 20, 21, 25, 26, 52–55. Furthermore, the Specification of the '908 patent discloses that CRF1 receptor antagonists were known in the art, identifies an example of a CRF1 receptor antagonist, and provides an exemplary embodiment by which a CRF1 receptor antagonist is administered to achieve the claimed effect. See Ex. 1001 col. 10, ll. 47–64, col. 12, ll. 27–30; Ex. 4. Finally, Petitioner's declarant, Dr. Carey, acknowledges that this genus would have been well known to a

person of ordinary skill in the art. *See* Ex. 1005 ¶ 99 (citing Ex. 1029; Ex. 1018; Ex. 1030; Ex. 1031) ("Based on my review of the published literature, over 100 CRF1 receptor antagonists had been characterized or were in clinical development prior to the filing of the '908 patent, including NBI34041, verucerfont, and pexacerfont").

We consequently conclude that Petitioner's argument has not established that the Specification fails to "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351. We further conclude that Petitioner has not demonstrated that it is more likely than not that any claim in Ground IV is unpatentable.

G. Ground V: Claims 1–25 Lack of Enablement

1. Petitioner's Contentions

Petitioner argues that the Specification of the '908 patent fails to enable the full scope of the claims, because the claims recite CRF1 receptor antagonists broadly, but the patent provides only a single example, tildacerfont (Compound 1). Pet. 76. Petitioner contends that, during prosecution, Patent Owner singled out tildacerfont by alleging that tildacerfont's ability to maintain the claimed ACTH and 17-OHP reductions were unexpected. *Id.* (citing Ex. 1002, 30–38). Petitioner further contends that Patent Owner relied on this argument to distinguish another CRF1 receptor antagonist, Neurocrine's NBI-77860. *Id.*

Petitioner argues that the genus of CRF1 receptor antagonists included over 100 structurally diverse compounds prior to the filing of the '908

patent. Pet. 76 (citing Ex. 1005 ¶ 99). Petitioner asserts that, given the large scope of the CRF1 receptor antagonist genus, and given Patent Owner's arguments that the ability of a single agent (tildacerfont) to perform the claimed reduction was unexpected relative to a different CRF1 receptor antagonist, Spruce fails to enable the full scope of the claims. *Id.* According to Petitioner, it would require undue experimentation to determine which CRF1 receptor antagonists from among the members of this large genus could achieve the claimed reductions. *Id.* at 76–77.

2. Patent Owner's Preliminary Response

Patent Owner responds that Petitioner offers only the conclusory assertion that the claims would require undue experimentation, but presents no evidence to support this assertion. Prelim. Resp. 44. Patent Owner asserts that Petitioner's declarant fails to address the issue of whether the claims would require undue experimentation. *Id.*

Patent Owner asserts that the Specification of the '908 patent provides an explanation of the mechanism of action, a working example, and clinical trial protocols used to verify efficacy. Prelim. Resp. 46. Patent Owner argues that Petitioner ignores the Specification's explanation that CAH is treated by "reducing the elevated ACTH levels from the pituitary," its identification of CRF1 as "the major physiological regulator of the basal and stress-induced release of adrenocorticotropic hormone ('ACTH')," and its description of the development of "biologically-active small molecules having significant CRF receptor binding activity and which are capable of antagonizing the CRF1 receptor" to reduce ACTH levels by reducing CRF

secretion. *Id.* at 46–47 (citing Ex. 1001 cols. 10–11, ll. 66–9, col. 11, ll. 49–64).

Patent Owner further contends that Petitioner ignores the '908 patent's provision of the protocols used for evaluating CRF1 receptor antagonists for treatment of CAH. Prelim. Resp. 47 (citing Ex. 1001 cols. 36–48, ll. 35–3). According to Patent Owner, Petitioner unduly minimizes the importance of the working example and the fact that a relatively small number (approximately 100) of known compounds were already available. *Id.* Patent Owner argues that the '908 patent "disclosure provides considerable direction and guidance on how to practice their invention and presents working examples" and thus "leads to the conclusion that undue experimentation would not be required to practice the invention." *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988). Patent Owner asserts that the petition provides no reason that a skilled artisan, equipped with the protocols of the '908 patent and the discrete genus of CRF1 receptor antagonists, would require undue experimentation to make and use the claimed invention. Prelim. Resp. 47. Patent Owner notes that the Specification is not required to demonstrate experimentally every possible embodiment that falls within the scope of a claim in order to be enabling. *Id.* (citing *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1336 (Fed. Cir. 2003)).

Finally, Patent Owner argues, Petitioner contends that the art was unpredictable because one CRF1 receptor antagonist performed differently relative to another CRF1 receptor antagonist. Prelim. Resp. 48 (citing Pet. 76). However, argues Patent Owner, differing levels of performance for one compound does not undermine enablement. *Id.* Patent Owner asserts that "[e]ven if some of the claimed combinations were inoperative, the

claims are not necessarily invalid." *Id.* (quoting *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984)) (alteration in original).

3. Analysis

Section 112 requires that the patent specification enables "those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'" in order to extract meaningful disclosure of the invention and, by this disclosure, advance the technical arts. *Koito Mfg. Co., Ltd. v. Turn-Key-Tech, LLC*, 381 F.3d 1142, 1155 (Fed. Cir. 2004) (quoting *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997)). Furthermore:

> The scope of [patent] claims must be less than or equal to the scope of the enablement. The scope of enablement, in turn, is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation.

Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc., 166 F.3d 1190, 1196 (Fed. Cir. 1996); *see also In re Goodman*, 11 F.3d 1046, 1050 (Fed. Cir. 1993) (holding that "the specification must teach those of skill in the art 'how to make and how to use the invention as broadly as it is claimed'"). Furthermore, "the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970).

Petitioner argues that the claims of the '908 patent are not enabled because a person of ordinary skill in the art would be required to perform

"undue experimentation" in order to practice the invention. Pet. 76–77 (citing *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)).[6] Petitioner provides no evidence of record to support this allegation, beyond noting that, during prosecution, Patent Owner contended that tildacerfont's ability to maintain the claimed ACTH and 17-OHP reductions was unexpected, distinguishing it from another CRF1 receptor antagonist, Petitioner's NBI-77860. *Id.* at 76.

We do not find this persuasive. In the Notice of Allowance, filed September 30, 2020, the Examiner provided two reasons why the Specification of the '908 patent discloses unexpected results: (1) hormone reductions were maintained over a 6-week period in the treatment of congenital adrenal hyperplasia; and (2) maintaining the reduced hormone levels beyond 24 hours post-treatment. *See* Ex. 1002, 12. Nevertheless, the Examiner made no finding that the claims of the '908 patent were not enabled by the Specification.

More importantly, Petitioner adduces no evidence of record that practicing the invention claimed by the '908 patent would require undue experimentation. To the contrary, Petitioner's declarant, Dr. Carey, testifies that the genus of CRF1 receptor antagonists was known in the art. The prior art reference principally relied upon by Petitioner, Grigoriadis, expressly teaches significant reduction of ACTH and 17-OHP levels in humans in response to administration of another known CRF1 receptor antagonist, verucerfont, compared to placebo. *See* Ex. 1006 ¶¶ 90–95. The

[6] We also note here that, although Petitioner cites to *Wands*, the Petition provides no systematic analysis of, or even addresses, the *Wands* factors in the context of this case.

Specification of the '908 patent discloses, as Patent Owner points out, an explanation of the mechanism of action, a working example, and clinical trial protocols used to verify efficacy. *See* Prelim Resp. 46. Against these disclosures, we find that Petitioner's argument that practicing the claimed invention of the '908 patent would require undue experimentation, without further evidentiary support, would be unsustainable at trial. We consequently conclude that Petitioner has failed to establish that it is more likely than not that any claim in Ground V is unpatentable. We therefore deny institution of post grant review.

IV. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has failed to establish a sufficiently persuasive showing that the cited prior art references disclose, teach, or suggest at least one claim of the '908 patent, as set forth in the asserted Grounds I–III or that the claims lack written descriptive support or are not enabled as set forth in the asserted Grounds IV and V respectively. 35 U.S.C. § 314. Because we decline to institute post-grant review on the merits, we do not reach Patent Owner's arguments with respect to our discretion to deny institution under 35 U.S.C. § 325(d).

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED, pursuant to 35 U.S.C. § 314(a), that the Petition for post-grant review of the challenged claims of US Patent 10,849,908 B2 is DENIED with respect to all Grounds in the Petition; and

FURTHER ORDERED that post-grant review is not instituted.

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