

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEUROCRINE BIOSCIENCES, INC.,
Petitioner,

v.

SPRUCE BIOSCIENCES, INC.,
Patent Owner.

PGR2022-00025
Patent 11,007,201 B2

Before JOHN G. NEW, SUSAN L. C. MITCHELL, and TINA E. HULSE,
Administrative Patent Judges.

MITCHELL, *Administrative Patent Judge.*

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

I. INTRODUCTION

On February 18, 2002, Neurocrine Biosciences, Inc. (“Petitioner”) filed a Petition for Post-Grant Review of claims 1–19 of U.S. Patent No. 11,007,201 B2 (Ex. 1001, “the ’201 patent”). Paper 1 (“Pet.”). On June 17, 2022, Spruce Biosciences, Inc. (“Patent Owner”) filed a Preliminary Response. Paper 6 (Prelim. Resp.).

Petitioner requested leave to file a reply brief addressing Patent Owner’s arguments in its Preliminary Response, which we granted along with authorization for Patent Owner to file a sur-reply in response. *See* Paper 7. On July 14, 2022, Petitioner filed its Reply, *see* Paper 8 (“Reply”), and on July 28, 2022, Patent Owner filed its Sur-Reply, *see* Paper 9 (“Sur-Reply”). On September 15, 2022, we denied institution of post-grant review. *See* Paper No. 10.

On October 13 2022, Petitioner filed a Rehearing Request, and Petitioner additionally filed a request for Precedential Opinion Panel (“POP”) review. *See* Papers 11, 12. On July 20, 2023, the Director *sua sponte* initiated Director Review of our decision, *see* Paper 13, and ordered dismissal of the requests for rehearing and POP review, *see* Paper 14. On August 4, 2023, the Director issued a decision vacating our decision denying institution and remanding the case to the panel “for further proceedings consistent with my Decision in PGR2021-00088.” Paper 15.

Institution of post-grant review is authorized by statute only when “the information presented in the petition . . . demonstrate[s] 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; *see* 37 C.F.R. § 42.4. Upon considering the Petition, Patent Owner Preliminary Response, and the cited evidence in light

of the Director’s Decision, we conclude that Petitioner has satisfied its burden under 35 U.S.C. § 324 to show that it is more likely than not that at least 1 of the claims challenged in the Petition is unpatentable. Therefore, we grant institution of a post-grant review.

A. Real Parties in Interest

Petitioner identifies itself as the real party in interest. Pet. 82. Patent Owner also identifies itself as the real party in interest. Paper 3, 2.

B. Related Matters

Petitioner asserts that it “is not aware of any disclaimers, reexamination certificates, or petitions for *inter partes* or post grant review for the ’201 Patent, nor is Petitioner aware of any pending civil actions involving the ’201 patent.” Pet. 82.

Petitioner does identify PGR2021-00088 in which Petitioner sought post-grant review of the parent patent for the ’201 patent, the U.S. Patent No. 10,849,908 B2 (“the ’908 patent”). Pet. 82. Patent Owner also identifies PGR2021-00088. *See* Paper 3, 2.

C. The ’201 Patent (Ex. 1001)

The ’201 patent, titled “Corticotropin Releasing Factor Receptor Antagonists,” issued May 18, 2021, identifying Patent Owner as the applicant and assignee. Ex. 1001, codes (54), (71), (72). The ’201 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 methods of using the same for the

treatment of congenital adrenal hyperplasia (“CAH”).” Ex. 1001, Abstr., 1:32–60.

Relevantly, the ’201 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 corticotrophic hormone (“ACTH”) by the secretory cells of the adenohypophysis, for the treatment of CAH. Ex. 1001, 10:47–12:25. The Specification of the ’201 patent explains the necessity of controlling the level of ACTH to prevent the overproduction of androgens, such as androstenedione (“A4”). *Id.* at 11:65–12:25, 48:3; *see also id.* at 43:47–53 (explaining in Example 4 that “Compound 1 attenuates morning rise in A4 which indicates an ability to control excess androgen production and associated symptoms (*see* FIG. 4)”).

D. Challenged Claims

Petitioner challenges all nineteen claims of the ’201 patent. Pet. 1, 4. All claims of the ’201 patent are method claims. Claim 1 is the sole independent claim. Claims 2–5, 7, and 9–18 depend directly from claim 1, claim 6 depends from claim 5, claim 8 depends from claim 7, and claim 19 depends from claim 18.

Claim 1 is representative and reproduced below:

1. A method of treating congenital adrenal hyperplasia (CAH) in a human comprising administering to the human a therapeutically-effective amount of a CFR₁ receptor antagonist or a pharmaceutically acceptable salt thereof, wherein an androstenedione (A4) level in the human is reduced from baseline and is maintained at a reduced level post 24 hours.

Ex. 1001, 47:51–48:5.

E. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–19 of the ’201 patent on the following grounds, *see* Pet. 4:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–4, 7–9, 11–15, 18	102 ¹	Grigoriadis ²
10, 16, 17, 19	103	Grigoriadis
5, 6	103	Grigoriadis and Romano ³
1–4, 7–19	103	Grigoriadis and Turcu 2016 ⁴
5–6	103	Grigoriadis, Turcu 2016, and Romano
1–19	112	Lack of written description

Petitioner submits the Declaration of Robert M. Carey, M.D. (Ex. 1005) in support of institution of post-grant review.

¹ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. §§ 102, 103, and 112, effective March 16, 2013. Because the earliest application on which the ’201 patent claims priority was filed after the effective date of the AIA, we apply the AIA version of 35 U.S.C. §§ 102, 103, 112. *See* Ex. 1001, codes (22), (60), (63).

² Dimitri E. Grigoriadis, US 2017/0020877 A1, published Jan. 26, 2017 (Ex. 1006, “Grigoriadis”).

³ Steve Romano, US 2005/0209250 A1, published Sept. 22, 2005 (Ex. 1007, “Romano”).

⁴ Adina F. Turcu, et al., *Single-Dose Study of a Corticotropin-Releasing Factor Receptor-1 Antagonist in Women with 21-Hydroxylase Deficiency*, 101 J. CLIN. ENDOCRINOL. METAB. 1174–1180 (2016) (Ex. 1008, “Turcu 2016”).

II. ANALYSIS

A. Eligibility for Post-Grant Review

The post-grant review provisions set forth in Section 6(d) of the AIA apply only to patents subject to the first-inventor-to-file provisions of the AIA. *See* AIA § 6(f)(2)(A) (“The amendments made by subsection (d) . . . shall apply only to patents described in section 3(n)(1).”). Patents subject to the first-inventor-to-file provisions are those that issue from applications “that contain[] or contained at any time . . . a claim to a claimed invention that has an effective filing date as defined in section 100(i) of title 35, United States Code, that is on or after” March 16, 2013. *Id.* § 3(n)(1). Our rules require that each petitioner for post-grant review certify that the challenged patent has an effective filing date that renders the patent available for post-grant review. 37 C.F.R. § 42.204(a) (“The petitioner must certify that the patent for which review is sought is available for post-grant review.”). In addition, “[a] petition for a post-grant review may only be filed not later than the date that is 9 months after the date of the grant of the patent or of the issuance of a reissue patent (as the case may be).” 35 U.S.C. § 321(c); *see also* 37 C.F.R. § 42.202(a) (accord).

Petitioner states the following.

Neurocrine certifies that the ’201 Patent is available for PGR. The present petition is being filed within nine months of the issuance of the ’201 patent on May 18, 2021. Neurocrine has not filed a civil action challenging the validity of any claim of the ’201 patent. Neurocrine is not barred or estopped from requesting this review challenging claims 1–19

Pet. 3.

On this record, we determine that the ’201 patent is eligible for post-grant review. Specifically, the application leading to the ’201 patent

was filed on October 22, 2020, and asserts that it is a continuation of the application that led to the '908 patent, which in turn claims priority to a previously filed PCT application and a provisional application, the first of which was filed on August 14, 2017. Ex. 1001, codes (22), (60), (63). All of these dates fall after March 16, 2013. Also, this Petition was filed on February 18, 2022, which is within nine months after the May 18, 2021, issue date of the '201 patent. *Id.* at code (45).

B. Person of Ordinary Skill in the Art

Factual indicators of the level of ordinary skill in the art include “the various prior art approaches employed, the types of problems encountered in the art, the rapidity with which innovations are made, the sophistication of the technology involved, and the educational background of those actively working in the field.” *Jacobson Bros., Inc. v. U.S.*, 512 F.2d 1065, 1071 (Ct. Cl. 1975); *see also Orthopedic Equip. Co. v. U.S.*, 702 F.2d 1005, 1011 (Fed. Cir. 1983) (quoting with approval *Jacobson Bros.*).

According to Petitioner, a person of ordinary skill in the relevant art (“POSA”) “would have 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 . . . [and] would also have at least three years of experience conducting research concerning endocrine disorders, including CAH or other adrenal disorders.” Pet. 26–27 (citing Ex. 1005 ¶ 34 (Dr. Carey Declaration)).

Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Preliminary Response. Because Petitioner’s definition of a person of skill in the art appears commensurate with the level

of skill reflected in the asserted art in this case as well as the '201 patent itself, *see, e.g.*, Exs. 1024, 1025, 2003, 2004, 2005, we apply Petitioner's proposed level of ordinary skill in the art to determine whether it is more likely than not that Petitioner would prevail with respect to at least one of the claims challenged in the Petition. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (stating prior art itself can reflect the appropriate level of ordinary skill in the art).

C. *Claim Construction*

We construe claims “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 (2019). Therefore, we construe the challenged claims under the framework set forth in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc). Under this framework, claim terms are given their ordinary and customary meaning, as would be understood by a person of ordinary skill in the art, at the time of the invention, in light of the language of the claims, the specification, and the prosecution history of record. *Id.* Only those terms that are in controversy need be construed, and only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co., Matal*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (citing *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

Petitioner proposes constructions for the claim terms “baseline/from baseline,” “human,” and “maintained at a reduced level post 24 hours [4 weeks or 6 weeks].” *See* Pet. 27–30. Patent Owner responds that “it is sufficient for the Board to maintain its decision in Petitioner's prior PGR [PGR2021-00088], rejecting Petitioner's argument that the claimed

reduction ‘from baseline’ is satisfied by the reduction relative to placebo in Grigoriadis, as also was established during prosecution.” Prelim. Resp. 16.

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 grant institution of post-grant review.

Petitioner points to clinical data in the ’201 patent regarding A4 in which the A4 level is measured “before the administration of tildacerfont, a CRF1 receptor antagonist, and measuring A4 level after the administration of the first dose of tildacerfont.” Pet. 27–28. Petitioner also notes that “Figure 4 of the ’201 patent presents the measurements and shows a reduction of A4 due to the administration of tildacerfont, i.e., a change from baseline.” *Id.* at 28. In line with these teachings, Petitioner asserts that it applies the definition of “from baseline” as “a measurement made prior to, and/or at the beginning of, administration of the drug.” *Id.*; see Ex. 1005 ¶ 38.

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. 15–16 (stating “Petitioner simply assumes that a reduction from placebo amounts to a reduction from baseline”). Patent Owner argues that the prosecution history of the ’201 patent, including the prosecution history of its parent patent, the ’908 patent, is part of the intrinsic evidence of the claims’ meaning, if in evidence, which it is here. *Id.* at 16 (citing *Phillips*, 415 F.3d at 1317); see Exs. 1002, 1037.

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. 16–17 (citing Pet. 21). Patent Owner 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.* at 17 (*see* Ex. 1037, 36–37). 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 17 (quoting Ex. 1037, 36–37) (emphasis omitted). Patent Owner contends that Applicants explained, 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 from baseline. *Id.* at 17 (citing Ex. 1037, 100).

Independent claim 1 recites a method of treating CAH by reducing an A4 level “from baseline” after administering a CRF₁ receptor antagonist to a CAH patient. *See* Ex. 1001, 47:51–48:5. 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, 41:55–59. 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 '201 patent. *See*

Ex. 1037, 36–37. We note that placebos were evidently not employed in the phase 2 clinical study of Example 4.⁵

Given the sole exemplary description of “baseline” in Example 4 of the Specification, we construe the claim term reciting “reduced from baseline” as meaning “a reduction in A4 level compared to an A4 level measurement made prior to, and/or at the beginning of, administration of the drug.”

D. Ground 1 – Anticipation by Grigoriadis

Petitioner asserts that claims 1–4, 7–9, 11–15, and 18 are anticipated by Grigoriadis, and sets forth how each limitation is met by Grigoriadis. As support, Petitioner cites the Declaration of Dr. Carey. *See* Pet. 42–51; Ex. 1005 ¶¶ 47–56.

1. Overview of Grigoriadis (Ex. 1006)

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.* ¶ 4. Grigoriadis teaches that:

Corticotropin-releasing factor (CRF)⁶ activates the CRF₁ 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 CAH, thereby allowing

⁵ 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.

⁶ The terms “corticotropin releasing factor” (CFR) and “corticotropin releasing hormone” (CRH) as used herein are synonymous.

normalization of androgen production while using lower, more physiologic doses of hydrocortisone, and reducing treatment-associated side effects.

Id. ¶ 6.

Grigoriadis lists several CRF₁ receptor antagonists including SSR-125543 that Petitioner asserts is crinecerfont and NBI-77860 that Patent Owner asserts is verucerfont. *See, e.g.*, Ex. 1006 ¶¶ 13, 51, 54; Pet. 32, 43; Prelim. Resp. 2, 8. Grigoriadis, however, only teaches administering NBI-77860 or verucerfont to a CAH patient as shown in Example 6. *See* Ex. 1006 ¶¶ 90–95; Pet. 39–40; Prelim. Resp. 44.

Example 6 of Grigoriadis teaches a clinical study titled “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.” Ex. 1006 ¶ 90. This study comprised a single-blind, placebo-controlled, single center, fixed-sequence single-dose clinical trial in adult female classical CAH patients, designed to “assess the safety, tolerability, and plasma exposure of NBI-77860 [verucerfont], as well as the effect of this compound on endogenous levels of HPA [or hypothalamic-pituitary-adrenal] axis hormones.” *Id.*

The dosage regimen and experimental design of this study is depicted in Figure 4 of Grigoriadis reproduced below.

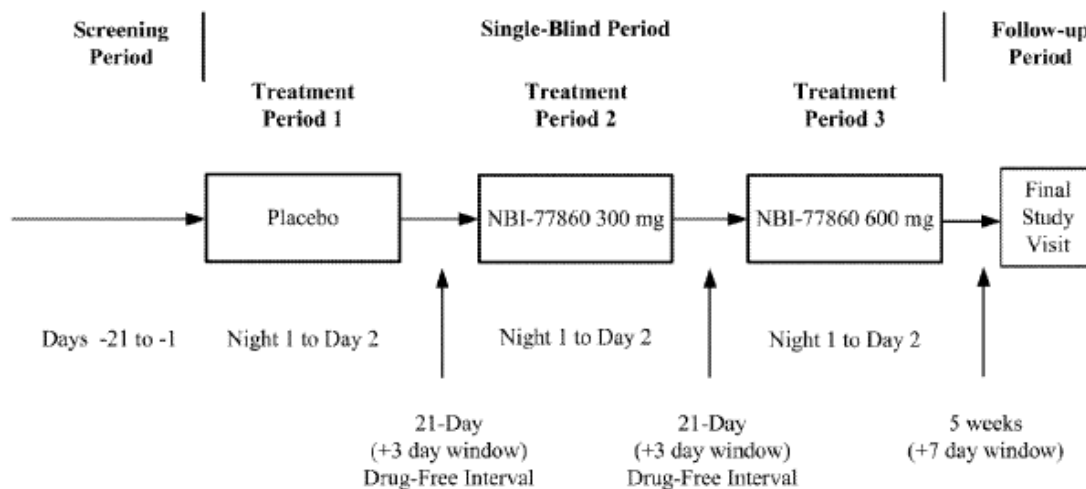


FIG. 4

Figure 4 of Grigoriadis set forth above shows 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 CAH were administered single bedtime doses (HS) of . . . placebo and verucerfont 300 mg, and 600 mg during three separate treatment periods. Ex. 1006 ¶ 91. The usual morning dose of concurrent steroidal treatment for the eight subjects was delayed until after the 16-hour post-dose blood samples were collected. *Id.* The results of the study are depicted in Figure 5 of Grigoriadis reproduced below.

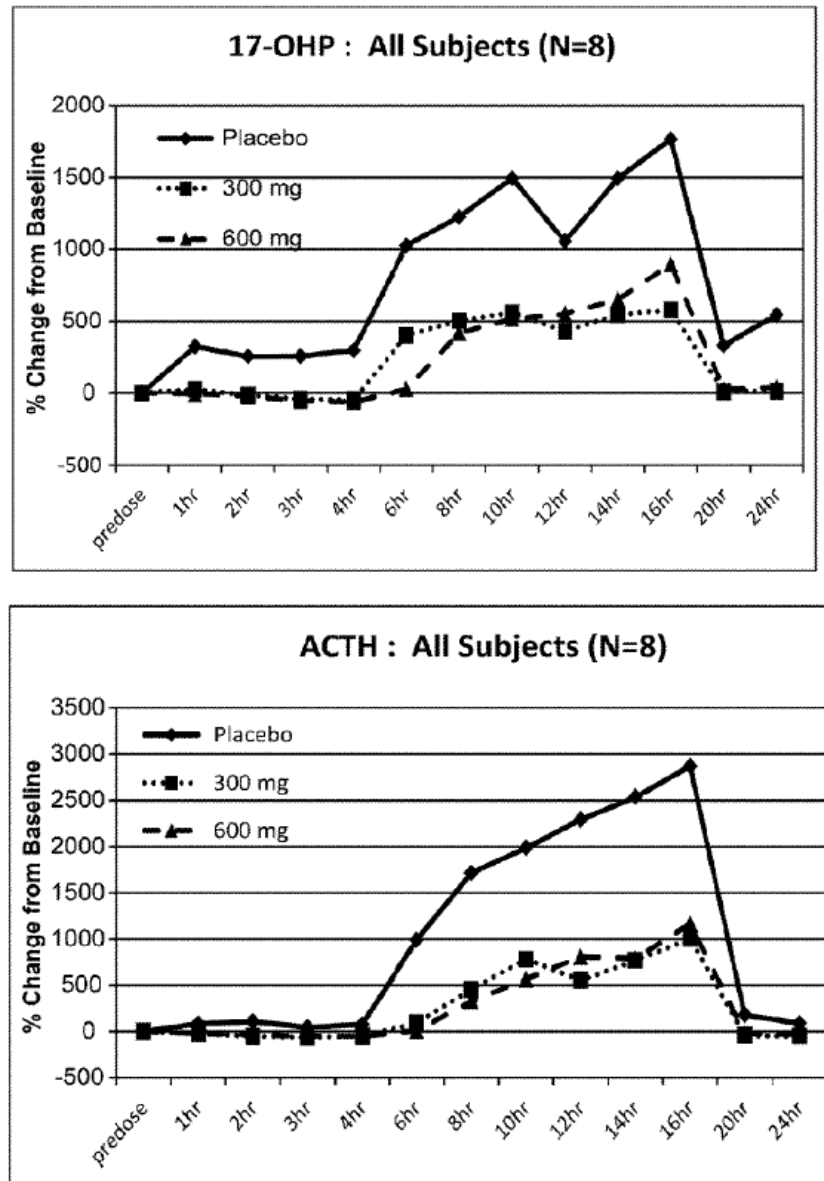


FIG. 5

Figure 5 of Grigoriadis depicts levels of 17-OHP and ACTH in response to placebo, 300 mg dose of verucerfont, and 600 mg dose of verucerfont during the 24-hour post-dose periods. Ex. 1006 ¶ 92. Grigoriadis concludes the following.

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. Principles of Law

To show anticipation under § 102, each and every claim element, arranged as in the claim, must be found in a single prior art reference. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359 (Fed. Cir. 2008). The prior art need not, however, use the same words as the claims in order to find anticipation. *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009). It is also permissible to consider not only the literal teachings of the prior art reference, but also the inferences an ordinarily skilled person would draw from the reference. *Eli Lilly and Co. v. Los Angeles Biomedical Res. Inst. at Harbor-UCLA Med. Ctr.*, 849 F.3d 1073, 1074–75 (Fed. Cir. 2017); *In re Preda*, 401 F.2d 825, 826 (CCPA 1968).

A reference may also anticipate a claim even if it does not expressly teach all the limitations arranged or combined as in the claim, “if a person of skill in the art, reading the reference, would ‘at once envisage’ the claimed arrangement or combination.” *Microsoft Corp. v. Biscotti, Inc.*, 878 F.3d 1052, 1068 (Fed. Cir. 2017) (quoting *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015)).

To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the

reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. . . . This modest flexibility in the rule that “anticipation” requires that every element of the claims appear in a single reference accommodates situations where the common knowledge of technologists is not recorded in the reference

Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268–69 (Fed. Cir. 1991); *see also In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981) (“Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.”) (quoting *Hansgird v. Kemmer*, 102 F.2d 212, 214 (CCPA 1939)).

3. Independent Claim 1

a. Petitioner’s Arguments

As in the petition challenging the claims of the ’908 patent, Petitioner again here relies on the disclosure of crinecerfont in Grigoriadis as “a CRF1 receptor antagonist, [that is] useful for the treatment of CAH,” combined with a clinical study reported in Auchus 2021⁷ to show that the “administration of a therapeutically effective amount of crinecerfont to a patient as taught in Grigoriadis *inherently and necessarily* results in a reduction of a patient’s A4 level compared to the patient’s baseline level, and that reduction is maintained post 24 hours.” Pet. 43 (emphasis added). Petitioner explains its inherency analysis as follows.

⁷ Richard J. Auchus et al., *Crinecerfont Lowers Elevated Hormone Markers in Adults With 21-Hydroxylase Deficiency Congenital Adrenal Hyperplasia*, 20 J. CLIN. ENDOCRINOL. METAB. 1–12 (2021) (Ex. 1009, “Auchus 2021”).

[A] skilled artisan would understand “maintained at a reduced level post 24 hours” to mean maintenance of reduced hormone levels for more than 24 hours when a patient is dosed repeatedly. After 14 days of administering crinecerfont once or twice daily, a patient, and indeed most patients, in the clinical study reported in Auchus 2021 experienced a reduction in A4 levels at Day 14 compared to baseline measurements. Specifically, median A4 measurements taken over 24 hours and within the morning window (6-10 a.m.) time points showed that administration of a therapeutically effective amount of crinecerfont to a patient meets the reduction in A4 level from baseline requirement recited in ’201 patent claim 1 at Day 14, *i.e.*, post 24 hours. Baseline measurement[s] were taken over a 24-hour period beginning in the evening of the seventh day before the study began (Day-7 to Day-6), and thus were made prior to administration of the study drug.

Administration of a therapeutically effective amount of crinecerfont to a patient, as taught by Grigoriadis, necessarily results in a reduction in a patient’s A4 level from baseline after 14 days of repeated dosing—*i.e.*, the A4 reduction is maintained for more than 24 hours. Thus Grigoriadis inherently anticipates ’201 patent claim 1.

Pet. 43–44 (citing Ex. 1005 ¶¶ 43–56; Ex. 1006 ¶¶ 54, 63; Ex. 1009, 3–11, Tables 2–3, Figs. 2–4).

b. Patent Owner’s Arguments

Patent Owner contends, first, that Auchus 2021 is an improper submission under 37 C.F.R. § 42.65(b). Patent Owner further argues that Auchus 2021 does not demonstrate that Grigoriadis inherently discloses the required reduction from baseline. Prelim. Resp. 38–47.

With respect to its first argument, Patent Owner notes that Auchus 2021 is a document containing self-funded data produced by Petitioner’s employees. Prelim Resp. 39. Patent Owner explains that Rule 42.65(b) requires that a party relying on a technical test or data from such a test must

provide an affidavit explaining (1) why the test or data is being used, (2) how the test was performed and data generated, (3) how the data is used to determine a value, (4) how the test is regarded in the relevant art, and (5) any other information necessary for the Board to evaluate the test and data. *Id.*; see 37 C.F.R. § 42.65(b). Patent Owner asserts that no such affidavit has been submitted by Petitioner. *Id.* at 40.

Patent Owner argues further that the Carey Declaration, upon which Petitioner relies, does not provide the information required by Rule 42.65(b). Prelim. Resp. 40. Patent Owner contends that: (1) Dr. Carey’s Declaration does not address why baseline readings are being used in Auchus 2021 (as opposed to the placebo readings of Grigoriadis); (2) Dr. Carey is not an author of Auchus 2021 and does not testify that he has personal knowledge of how the test was performed and the data generated (as opposed to simply reading what is written in the document itself); (3) Dr. Carey asserts that Auchus 2021 reveals a reduction in hormone levels relative to baseline for some patients (citing Ex. 1005 ¶¶ 51, 56), but fails to describe how the data was used to determine this alleged finding; (4) Dr. Carey does not describe how the test is regarded in the relevant art because it simply repeats excerpts of Auchus 2021 and then opines that the test “was a well-designed study”; and (5) Dr. Carey fails to provide the data underlying the experiments summarized in Auchus 2021 or even testify that he has examined it. *Id.* at 40–41 (citing 37 C.F.R. § (42.65(a)).

Patent Owner argues that the purpose of Rule 42.65 is “to ensure that a party proponent meets a threshold level of reliability when offering technical tests and data as evidence.” Prelim. Resp. 41 (citing *3D-Matrix, LTD v. Menicon Co., LTD*, IPR2014-00398, Paper 11, at 9 (Aug. 1, 2014)).

Patent Owner contends that Petitioner's failure to provide a knowledgeable affiant who can satisfy the requirements of Rule 42.65 does not provide the indicia of threshold reliability required to accept this data as evidence and is highly prejudicial at least in that it improperly insulates Auchus 2021's data vetting through cross-examination of a witness with first-hand knowledge regarding the data and the experiments. *Id.*

Patent Owner's second argument asserts that Petitioner fails to establish inherent anticipation because Petitioner fails to address material differences between the methodologies of Auchus 2021 and Grigoriadis. Prelim. Resp. 42. Patent Owner asserts that "[t]he petition again contends that Auchus 2021 evidences that Grigoriadis inherently discloses the claimed reduction of baseline hormone levels." *Id.* at 42–43. But, Patent Owner asserts, Auchus 2021 does not replicate Grigoriadis. *Id.* According to Patent Owner, Auchus 2021 discloses administering a different drug to a different cohort, using a different dosing regimen than what was evaluated in Grigoriadis. *Id.* at 43. Patent Owner argues that Auchus 2021 is a completely different study, and one that sheds no light on the method actually addressed in Grigoriadis. *Id.*

Patent Owner summarizes the differences between Grigoriadis and Auchus 2021 in the table reproduced below:

Grigoriadis	Auchus 2021
Treatment period: 1 day. EX1006, ¶90, FIG. 4.	Treatment period: 14 days. EX1009, 1.
Study drug: verucerfont (NBI-77860). EX1006, ¶90.	Study drug: crinecerfont (NBI-74788). EX1009, 1.
Placebo administered before study drug. EX1006, ¶90.	No placebo administered before study drug. EX1009, 2-3.
Patients: all female. EX1006, ¶91.	Patients: 11 women, 7 men. EX1009, 4-5.
Dose size: 300, 600 mg. EX1006, ¶91.	Dose size: 50-100 mg. EX1009, 2-3.
Dosing regimen: single dose at bedtime. EX1006, ¶91.	Dosing Regimen: 14 consecutive days of single dose or twice daily EX1009, 3.

Prelim. Resp. 43–44.

Patent Owner contends that Grigoriadis discloses a single-dose study of verucerfont (NBI-77860), which was administered to eight women as a single dose of 300 mg or 600 mg after placebo administration. Prelim. Resp. 44 (citing Ex. 1006 ¶¶ 90–93). By contrast, explains Patent Owner, Auchus 2021 discloses administration of crinecerfont (NBI-74788) to a cohort of men and women for 14 consecutive days at doses of between 50 mg/day to

100 mg/2x daily. *Id.* at 44 (citing Ex. 1009, 1–2). Patent Owner argues that Auchus 2021 does not disclose administering or evaluating verucerfont, and employs a different protocol than that employed by Grigoriadis. *Id.* at 32. Patent Owner contends that the Petition fails to address any of these differences, or demonstrate that Auchus 2021 provides proof of the inherency of Grigoriadis’ method. *Id.*

Patent Owner asserts that Petitioner may not prove inherency of Grigoriadis’ method using a methodology that does not faithfully follow the methodology of Grigoriadis. Prelim. Resp. 45 (citing Ex. 2009, 16–21, *see also, e.g., Valeant Int’l (Barbados) SRL v. Watson Pharm., Inc.*, No. 10-20526-CIVMORE, 2011 U.S. Dist. LEXIS 128742, at *14 (S.D. Fla. Nov. 7, 2011); *Glaxo, Inc. v. Novopharm Ltd.*, 830 F. Supp. 871, 876 (E.D.N.C. 1993), *aff’d*, 52 F.3d 1043 (Fed. Cir. 1995)). Patent Owner argues that the differing methodologies of Grigoriadis and Auchus 2021 fatally undermine Petitioner’s inherency argument. *Id.* at 46. Patent Owner states: “All Auchus 2021 shows is that administration of different doses of a different compound **for 14 consecutive days** to a different population than in Grigoriadis provided different results than were obtained in Grigoriadis.” *Id.* at 46 (citing Ex. 1009, 1–2).

Patent Owner disputes Petitioner’s arguments that Grigoriadis: (1) discloses crinecerfont; and (2) elsewhere discloses CRF₁ receptor antagonists may be administered from 50–1000 mg. Prelim. Resp. 46 (citing Pet. 43). Similarly, Patent Owner states “Petitioner simply fails to support its argument that a single dose of 50–1000 mg would **inherently and necessarily** result in a reduction from baseline.” *Id.*

c. Analysis

The Director’s Decision in PGR2021-00088 as applied to the proceeding before us here finds that Petitioner has shown sufficiently on the preliminary record for purposes of institution that Grigoriadis discloses a method of treating CAH by administering a species of CRF₁ receptor antagonist (crinecerfont) within the claimed genus. *Neurocrine Biosciences, Inc. v. Spruce Biosciences, Inc.*, PGR2021-00088, Paper 16, 14 (PTAB Aug. 4, 2023) (“Director’s Decision”). Specifically, the Director’s Decision finds on the record before us that, as set forth by our reviewing court in *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005), Grigoriadis’ method of treating CAH by administering crinecerfont anticipates the broader genus claim of treating CAH by administering a CRF₁ receptor antagonist, so long as the remaining limitations are disclosed expressly or inherently. *Id.* at 8.

Consequently, the Director’s Decision remands to the Board to determine whether Petitioner’s extrinsic evidence, Auchus 2021, shows that crinecerfont necessarily, and thus inherently, reduces the level of A4 from baseline, and is maintained at a reduced level post 24 hours from baseline, when used as taught in Grigoriadis’ method of treating CAH. *See id.* at 14. We then turn to an analysis of whether Petitioner has established that it is more likely than not that Grigoriadis anticipates the challenged claims. *Id.*

Pursuant to the Director’s Decision, we first inquire as to whether, on the record before us, we determine that Petitioner has shown sufficiently that Auchus 2021 demonstrates that crinecerfont inherently reduces the level of A4 “from baseline and is maintained at a reduced level post 24 hours” when used as taught in Grigoriadis’ method of treating CAH. *See Dir. Dec.* 14.

A claim is unpatentable as anticipated under 35 U.S.C. § 102 only when “every element and limitation of the claim was previously described in a single prior art reference, either expressly or inherently, so as to place a person of ordinary skill in possession of the invention.” *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1082 (Fed. Cir. 2008). A reference may inherently anticipate 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). Thus, 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.” *Agilent Technologies, Inc. v. Affymetrix, Inc.*, 567 F.3d 1366, 1383 (Fed. Cir. 2009) (emphasis added).

Independent claim 1 of the '201 patent recites “[a] method of treating congenital adrenal hyperplasia (CAH) in a human comprising administering to the human a therapeutically-effective amount of a CRF₁ receptor antagonist or a pharmaceutically acceptable salt thereof.” Ex. 1001, claim 1. Claim 1 of Grigoriadis recites, in relevant part, “[a] method for treating Congenital Adrenal Hyperplasia (CAH) by administering to a subject in need thereof a CRF₁ receptor antagonist.” Ex. 1006, claim 1. Grigoriadis further discloses:

In general, the amount of a compound described herein, that is present in a dose ranges from about 0.1 mg to about 30 mg per kg weight of the subject. In certain embodiments, a single dose is about 50–1000 mg. The use of the minimum dose that is sufficient to provide effective therapy is usually preferred. Subjects may generally be monitored for therapeutic effectiveness by clinical evaluation and using assays suitable for the condition being treated or prevented, which assays will be

familiar to those having ordinary skill in the art and are described herein.

Id. ¶ 63. On the record before us, we determine that Grigoriadis thus teaches the administration of a therapeutically-effective amount of a CRF₁ receptor antagonist, as recited in claim 1 of the '201 patent. There appears to be little dispute between the parties that Grigoriadis discloses this limitation of claim 1 quoted above.

Claim 1 of the '201 patent, however, further recites “wherein an adrostenedione (A4) level in the human is reduced from baseline and is maintained at a reduced level post 24 hours.” Petitioner relies upon Auchus 2021 as demonstrating that Grigoriadis inherently teaches this limitation. *See* Pet. 43–44.

Auchus 2021 discloses an open-label, multiple-dose, phase 2 study that included men and women (18–50 years) with 21-hydroxylase deficiency (“21OHD”). Ex. 1009, Abstr., 2–3. “This phase 2, open-label study used a sequential-cohort design to evaluate the safety, tolerability, and efficacy of 4 different crinecerfont dosing regimens, each dosed for 14 days in adults with classic 21OHD.” *Id.* at 2–3. The four crinecerfont dosing regimens administered were 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, morning and evening (BID, Cohort 4).” *Id.* Crinecerfont, also known as NBI-74788 or SSR-125433, is a CRF₁ receptor antagonist expressly disclosed by Grigoriadis. *See* Ex. 1006 ¶ 54 (“In still another embodiment, the CRF₁ receptor antagonist is SSR-125543 [4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl) ethyl]-5-methyl-N-(2-propyn-1-yl)-2-thiazolamine; *see also* Ex. 1005 ¶ 28 (“SSR-125543 is also known as crinecerfont”).

Furthermore, Auchus 2021 discloses that its subjects were administered doses of crinecerfont of either 50 or 100 mg once or twice-daily (depending upon to which cohort the subject belonged), which is within the range of 50–1000 mg/day disclosed by Grigoriadis as being therapeutically effective. Ex. 1009, 3; Ex. 1006 ¶¶ 48 n.3, 66. Therefore, we find that Petitioner has shown sufficiently that Auchus 2021 teaches Grigoriadis's method of treating CAH.

Auchus 2021 concludes the following.

At baseline, the 24-hour plasma/serum concentration profile of ACTH, 17OHP, and androstenedione demonstrated the expected early morning increases starting around 04:00 and peaking around 8:00 to 10:00 in the morning (Fig. 2). Treatment with crinecerfont for 14 days led to substantial median reductions for ACTH, 17OHP, and androstenedione relative to baseline, especially during the morning window, across all cohorts (*see* Fig. 2). The decrease in androstenedione was most pronounced for cohort 4 (100 mg twice a day).

In all cohorts, median ACTH, 7OHP, androstenedione, testosterone (in women), and androstenedione/testosterone ratio (in men) were reduced from baseline to day 14 whether based on samples collected during the morning window (06:00–10:00) or the 24-hour sampling period (*see* Table 2).

Ex. 1009, 5; *see* Ex. 1005 ¶¶ 51–54. The relevant portion of Figure 2 of Auchus 2021 regarding serum androstenedione that is referenced above is set forth below.

C. Serum androstenedione, nmol/L

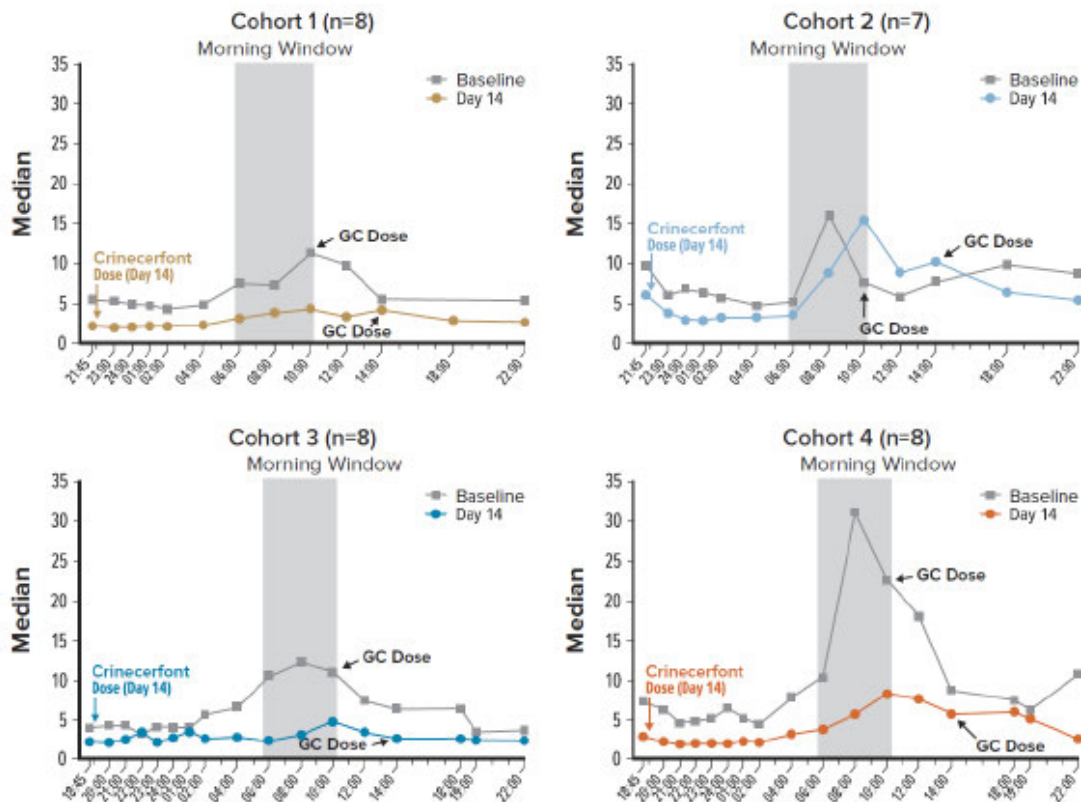


Figure 2. Twenty-four-hour profiles. For cohorts 1 and 2, crinecerfont dosing was at 22:00 on day 14; predose sampling was at 21:45. For cohorts 3 and 4, crinecerfont dosing was at 19:00 on day 14; predose sampling was at 18:45. 17OHR, 17-hydroxyprogesterone; ACTH, adrenocorticotropin; GC, glucocorticoid.

Ex. 1009, Fig. 2. These four graphs in Figure 2 compare baseline amounts of serum androstenedione to amounts after 14 days of treatment for the four cohorts in the Auchus 2021 study.

On the record before us, Petitioner has shown sufficiently that Auchus 2021 discloses that administration of what Grigoriadis states is an effective amount of crinecerfont, a CRF₁ receptor antagonist to a subject in need thereof (e.g., having CAH), as disclosed by Grigoriadis, necessarily, and therefore, inherently, results in achieving “an androstenedione (A4) level in the human is reduced from baseline and is maintained at a reduced level past 24 hours” as recited in claim 1.

We acknowledge that the challenged claims of the '201 patent are not expressly directed only to crinecerfont, but rather to the genus consisting of “CRF₁ receptor antagonist[s] or a pharmaceutically acceptable salt thereof.” Nevertheless, when the prior art discloses an anticipating species, it anticipates the genus to which that species belongs. *See Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985) (holding that “[i]t is also an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is “anticipated” if one of them is in the prior art” (quoting *In re Petering*, 301 F.2d 676, 682 (Fed. Cir. 1962))).

Based upon the record as presently developed, we do not find Patent Owner’s arguments persuasive to overcome Petitioner’s showing of anticipation for purposes of institution. Patent Owner argues that:

- (1) Auchus 2021 is an improper submission under 37 C.F.R. § 42.65(b); and
- (2) Auchus 2021 does not demonstrate that Grigoriadis inherently discloses the required reduction from baseline.

With respect to (1), Rule 42.65(b) requires that:

If a party relies on a technical test or data from such a test, the party must provide an affidavit explaining:

- (1) Why the test or data is being used;
- (2) How the test was performed and the data was generated;
- (3) How the data is used to determine a value;
- (4) How the test is regarded in the relevant art; and
- (5) Any other information necessary for the Board to evaluate the test and data.

As an initial matter, we do not find that Auchus 2021 is merely a “technical test or data from such a test.” The record before us suggests that

it is considerably more than that. It is a clinical research article published in the peer-reviewed⁸ scientific journal *The Journal of Clinical Endocrinology & Metabolism* on October 15, 2021. See Ex. 1005 ¶ 49. As such, it addresses most of the requisite factors of Rule 42.65(b) itself. For example, Rule 42.65 factors (2) and (3) are expressly addressed in the “Materials and Methods” sections entitled “Study Design and Participants,” “Procedures and Assessments,” and “Statistical Analysis.” See Ex. 1009, 2–4.

Furthermore, the Carey Declaration, submitted by Petitioner’s Declarant, also addresses the Rule 42.65(b) factors. See Ex. 1005 ¶¶ 49–56. Dr. Carey provides an extensive discussion of Auchus 2021, including factors (2) and (3) (as explained above). See *id.* at ¶¶ 49–56 (extensively discussing the experimental design of Auchus 2021, how its data was generated, and the nature and significance of the data obtained). Dr. Carey opines that Auchus 2021 “was a well-designed study” (factor (4)). *Id.* at ¶ 51. With respect to factor (1), Dr. Carey further testifies that:

The administration of crinecerfont to a patient with CAH, as taught by Grigoriadis, will result in a reduction of A4 level from the patient’s baseline level, which is maintained at a reduced level post 14 days. The reduction in A4 level of the patient will be at least 5% from baseline, at least 10% from baseline, at least 15% from baseline, at least 20% from baseline, and at least 25% from baseline, as recited in dependent claims 11-15 of the ’201 patent. The effect of the administration of crinecerfont on A4 levels in CAH patients was demonstrated by Neurocrine Biosciences in a Phase II

⁸ See *About The Journal of Clinical Endocrinology & Metabolism, Aims and Scope*, available at: <https://academic.oup.com/jcem/pages/About> (last visited November 28, 2023) (stating “*The Journal of Clinical Endocrinology & Metabolism* is the world’s leading peer-reviewed journal for the dissemination of original research as it relates to the clinical practice of endocrinology, diabetes, and metabolism”).

clinical study testing the effect of crinecerfont on a number of hormone biomarkers, including A4, in patients with 21-hydroxylase deficiency CAH.

Id. ¶ 48. This testimony addresses factor(1) of Rule 42.65(b). Furthermore, we find that Patent Owner’s argument that Dr. Carey was not involved in the Auchus 2021 study is irrelevant. Rule 42.65 has no such requirement. *Altaire Pharms., Inc. v. Paragon Biotech, Inc.*, 889 F.3d 1274 (2018).

Finally, we note that an alleged failure to comply with 37 C.F.R. § 42.65(b) goes to the weight given the evidence, and does not necessarily call for the exclusion of that evidence. *See EIS GmbH v. Novoluto GmbH*, IPR2020-00007 Paper 41 at 69 n.12 (citing *Emerson Elec. Co. v. IPCO, LLC*, IPR2017-00213, Paper 42, 25–26 (PTAB May 11, 2018) (affording expert testimony no weight for failure to comply with 37 C.F.R. § 42.65(b)); *Altair Pharm., Inc. v. Paragon Biotech, Inc.*, Paper 48, 16–17 (PTAB Nov. 14, 2016) (holding that “[w]ithout the necessary information prescribed in § 42.65(b), we cannot determine whether the evidence... is credible”). We find, based upon the record as presently developed, that Petitioner has shown sufficiently that the intrinsic disclosures of Auchus 2021, together with Dr. Carey’s testimony, are sufficient to meet the requirements of Rule 42.65(b).

With respect to Patent Owner’s argument (2), we find based upon the evidence presently before us, it too is unpersuasive. Contrary to Patent Owner’s argument, it is not the clinical study of Grigoriadis’ Example 6 that Auchus 2021 is required to replicate. Example 6 of Grigoriadis discloses only a single exemplary embodiment of the broader methods disclosed by Grigoriadis. Rather, the question presently before us is whether a person of ordinary skill in the art, practicing the method of Grigoriadis, would

necessarily, and therefore inherently, achieve the results disclosed by Auchus 2021, which are reflected in claim 1 of the '201 patent.

We have explained above why we find, based upon the evidence presently before us, that the method disclosed in the study of Auchus 2021 corresponds to the method recited by the claims in Grigoriadis.

Furthermore, we similarly find on the record before us that a person of ordinary skill in the art, following the method disclosed by Grigoriadis, and as disclosed by Auchus 2021, would necessarily achieve the results recited in challenged claim 1 of the '201 patent. We consequently conclude that, on the record as presently developed, Petitioner has demonstrated that it is more likely than not that Grigoriadis inherently discloses reducing the level of A4 “from baseline” and maintaining “a reduced level post 24 hours.”

We consequently conclude that, based upon the record as presently developed, Petitioner has demonstrated, for the purpose of this Decision, that it has demonstrated that it is more likely than not that Grigoriadis anticipates challenged claim 1 of the '201 patent. Patent Owner does not address the remaining dependent claims in Ground 1 apart from the arguments we addressed above. *See* Prelim. Resp. 38–47. Because we determine that Petitioner has shown that it is more likely than not that at least claim 1 is unpatentable as anticipated by Grigoriadis, we institute post-grant review of all challenged claims of the '201 patent, based on all of grounds identified in the Petition. *See SAS Inst., Inc. v. Iancu*, 138 S.Ct. 1348, 1359–60 (2018); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (interpreting the statute to require “a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition”).

E. Grounds 2–5 – Obviousness Grounds

In Ground 2, Petitioner asserts that claims 10, 16, 17, and 19 would have been obvious over the disclosure of crinecerfont in Grigoriadis and the knowledge of a skilled artisan. *See* Pet. 4, 51. In Ground 3, Petitioner asserts that claims 5 and 6 would have been obvious over the disclosure of crinecerfont in Grigoriadis, Romano, and the knowledge of a skilled artisan. Pet. 4, 55. In Ground 4, Petitioner asserts that claims 1–4 and 7–19 would have been obvious over Grigoriadis’ and Turcu 2016’s disclosure of NBI-77860 and the knowledge of a skilled artisan. Pet. 4, 57–72. In Ground 5, Petitioner asserts that claims 5 and 6 would have been obvious over the disclosure of NBI-77860 in Grigoriadis and Turcu 2016 along with Romano and the knowledge of a skilled artisan. *See* Pet. 4, 73.

For Grounds 2, 3, and 5, Patent Owner relies on its arguments discussed above for claim 1 as anticipated by Grigoriadis. *See* Prelim. Resp. 47–48, 53. We need not further address such arguments here.

For Ground 4, Patent Owner asserts that “Petitioner’s primary obviousness ground argues that Turcu—which addresses the very same study already described in Grigoriadis’s Example 6—evaluates A4 levels compared to placebo, and that this, in combination with Grigoriadis, rendered obvious the claimed reduction ‘from baseline.’ But Petitioner fails to show each and every element of the claimed invention is present in these references.” Prelim. Resp. 48 (citing Pet. 57–72). We have addressed the requirement of A4 levels “reduced from baseline” as required by claim 1 with regard to Grigoriadis in Ground 1. We will address this ground further after full development of the record at trial.

*F. Ground 6 – Unpatentability of Claims 1–19
for Lack of Written Description*

Petitioner asserts that claims 1–19 lack written description support because the '201 patent only discloses a single CRF₁ receptor antagonist, tildacerfont (Compound 1) and does not disclose structural features common to the CRF₁ receptor antagonists. Pet. 75–79.

The Director's Decision finds that as to written description, Petitioner has shown on this preliminary record that the '201 patent specification does not disclose a representative number of species falling within the scope of the recited genus of CRF₁ receptor antagonists that can be used in the claimed. *See* Dir. Dec. 15; *see also id.* at 10–15. The Director's Decision similarly finds that Petitioner has shown on the record as presently developed that the '201 patent specification does not disclose structural features common to the members of the functional genus so that one of skill in the art can visualize or recognize the effective members of the genus of CRF₁ receptor antagonists. *Id.*

We incorporate by reference the reasoning of the Director's Decision and adopt it in this Decision. *See* Dir. Dec. 10–15. We consequently conclude that Petitioner has shown that, for the purposes of this Decision, that challenged claims 1–19 more likely than not lack written descriptive support.

G. Discretionary Denial of Institution under 35 U.S.C. § 325(d)

Finally, Patent Owner urges us to exercise our discretion and deny institution under 35 U.S.C. § 325(d).

1. Legal standard

Under § 325(d), we have discretion to deny a petition that presents the same or substantially the same prior art or arguments as previously presented to the Office. *See* 35 U.S.C. § 325(d). In evaluating whether the factual predicate under § 325(d) is met, we consider a number of non-exclusive factors, as set forth in our decision in *Becton, Dickinson and 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”):

- (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.

Becton, Dickinson, IPR2017-01586, Paper 8 at 17–18.

In performing an analysis under § 325(d):

[T]he Board uses the following two-part framework: (1) whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same

arguments previously were presented to the Office; and (2) if either condition of 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. . . . If, after review of [*Becton, Dickinson*] factors (a), (b), and (d), it is determined that the same or substantially the same art or arguments previously were presented to the Office, then factors (c), (e), and (f) relate to whether the petitioner has demonstrated a material error by the Office.

Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential).

Consequently, we first turn to an analysis of *Becton, Dickinson* factors (a), (b), and (d) under this framework to determine 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.

2. Analysis

Patent Owner contends that Grigoriadis was considered and applied by the Examiner during prosecution of the '201 and '908 patents, and the Petition merely repeats the same and similar arguments to those already considered by the Office. Prelim. Resp. 26 (citing Ex. 1002, 20, 54–99, 202–212; Ex. 2009, 13–21). Patent Owner points to the Examiner's reasoning that Grigoriadis was considered to be the "the closest prior art," and yet allowed the claims over Grigoriadis because it discloses only a reduction relative to placebo and fails to disclose the required reduction relative to baseline. *Id.* at 26 (citing Ex. 1037, 12).

Specifically, Patent Owner argues that we should deny institution because, during prosecution of the '201 patent, "[t]he Examiner applied Grigoriadis as a basis for an obviousness rejection, noted that the

Grigoriadis/Turcu study did not disclose the claimed reduction from baseline, and ultimately concluded that the claims were patentable.” Prelim. Resp. 29 (citing Ex. 1002, 202–210). Patent Owner argues that Petitioner fails to demonstrate that the Examiner committed material error regarding the Grigoriadis/Turcu study and the Auchus study. *Id.* at 29–31.

We are not persuaded by Patent Owner’s argument that we should exercise our discretion to deny institution. Turning to the first part of the *Advanced Bionics* analysis, it is indisputable that Grigoriadis was extensively considered by the Examiner. *See, e.g.*, Exs. 1002, 1037. We disagree, however, with Patent Owner’s assertion that, in allowing the claims of the ’908 patent, the Examiner recognized Patent Owner’s argument concerning the patentable distinction between the placebo described in Grigoriadis and the baseline required by the claims of the ’908 patent. In the Notice of Allowance, the Examiner stated:

The Applicant has shown a reduction in the adrenocorticotrophic (ACTH) and 17-hydroxyprogesterone (17-OHP) hormone levels in humans, wherein said hormone reductions were maintained over a 6-week period, in the treatment of congenital adrenal hyperplasia. These results appear unexpected over the closest prior art, Grigoriadis et al.

Grigoriadis differs from the instant Invention in that Grigoriadis only discloses measuring ACTH and 17-OHP levels in individuals throughout the 24-hour post-dose period. The prior art does not disclose or suggest maintaining the reduced hormone levels beyond 24 hours post-treatment, let alone maintaining said reductions over a six week period.

Ex. 1037, 12 (internal citations omitted). Nevertheless, the fact remains that Grigoriadis was extensively considered by the Examiner during prosecution of the ’908 patent, although Patent Owner’s placebo-versus-baseline argument seems to have played no significant role in the prosecution history.

However, there is as yet no evidence of record that Auchus 2021 was ever considered by the Examiner. As we have explained in Section III.D.3.c. above, Auchus 2021 provides credible evidence that Grigoriadis inherently anticipates at least challenged claim 1 of the '201 patent. We have also explained why Patent Owner's argument that the differences in the studies disclosed by Example 6 of Grigoriadis and that disclosed by Auchus 2021 are not sufficient to overcome Petitioner's showing that challenged claim 1 of the '201 patent is inherently anticipated by Grigoriadis in view of the disclosures of Auchus 2021.

Because we find that Auchus 2021 was not considered by the Examiner as evidence of inherent anticipation of the challenged claims by Grigoriadis, we complete our § 325(d) analysis at the first step of the *Advanced Bionics* test.

Specifically, we find that there is a critical material difference between the asserted art (Auchus 2021 and Grigoriadis) and the prior art involved during examination (Grigoriadis only) (*Becton-Dickinson* factor (a)), and the cumulative nature of the asserted art (*Becton-Dickinson* factor (b)). Both Grigoriadis and Auchus 2021 are essential to Petitioner's theory of inherent anticipation. We further find that, because the Auchus 2021-based evidence of inherent anticipation was not considered during prosecution of the '201 patent, there exists insufficient overlap between the arguments made during examination and the manner in which Petitioner presently relies on the prior art (*Becton-Dickinson* factor (d)). We consequently end our *Advanced Bionics* analysis at the first step, and we decline to exercise our discretion to decline institution of post-grant review on this basis.

Moreover, because we conclude that denial of institution of post-grant review is unwarranted on this basis, we do not reach Patent Owner's argument that we should decline institution based upon Petitioner's alleged failure to demonstrate material error for written description or enablement. Prelim. Resp. 25–26.

III. CONCLUSION

For the foregoing reasons, we conclude that the information presented in the Petition has established that it is more likely than not that Petitioner will prevail in showing that challenged claims 1–19 of the '201 patent are unpatentable based on grounds presented in the Petition. Accordingly, we institute a post-grant review of claims 1–19 of the '201 patent.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 324(a), a post grant review of claims 1–19 of the '201 patent is *granted* with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that post-grant review is instituted.

PGR2022-00025
Patent 11,007,201 B2

FOR PETITIONER:

Dorothy Whelan
Robert Oakes
FISH & RICHARDSON P.C
whelan@fr.com
oakes@fr.com

FOR PATENT OWNER:

Michael T. Rosato
Jad A. Mills
WILSON SONSINI GOODRICH & ROSATI
mrosato@wsgr.com
jmills@wsgr.com