

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

WOCKHARDT BIO AG,
Petitioner,

v.

JANSSEN ONCOLOGY, INC.,
Patent Owner.

Case IPR2016-01582
Patent 8,822,438 B2

Before LORA M. GREEN, RAMA G. ELLURU, and
KRISTINA M. KALAN, *Administrative Patent Judges*.

KALAN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. INTRODUCTION

Wockhardt Bio AG (“Petitioner”) filed a Petition (Paper 4, “Pet.”) to institute an *inter partes* review of claims 1–20 of U.S. Patent No. 8,822,438 B2 (Ex. 1001, “the ’438 patent”) pursuant to 35 U.S.C. §§ 311–319. Janssen Oncology, Inc. (“Patent Owner”) filed a Preliminary Response (Paper 13, “Prelim. Resp.”). We instituted an *inter partes* review of claims 1–20 on certain grounds of unpatentability alleged in the Petition (Paper 28, “Dec.”).

After institution of trial, Patent Owner filed a Patent Owner Response (Paper 43, “PO Resp.”). Petitioner filed a Reply (Paper 54, “Reply”). An oral hearing was held on May 24, 2017. A transcript of the hearing has been entered into the record. Paper 71 (“Tr.”).

The Board has jurisdiction under 35 U.S.C. § 6. In this Final Written Decision, issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73, we determine that Petitioner has shown by a preponderance of the evidence that all claims of the ’438 patent for which trial was instituted, namely, claims 1–20, are unpatentable.

II. BACKGROUND

A. Related Matters

The parties indicate that the ’438 patent is being asserted in a number of district court proceedings, some of which have been terminated. Pet. 66; Paper 8, 2–4. Patent Owner represents that the following proceedings have not been terminated: *BTG Int’l Ltd. v. Actavis Labs. FL, Inc.*, C.A. No. 2:15-cv-05909-KM-JBC (D.N.J.), *Janssen Biotech, Inc. v. Mylan Pharms. Inc.*, C.A. No. 1:15-cv-00130-IMK (N.D. W. Va.), *BTG Int’l Ltd. v. Amerigen Pharms., Inc.*, C.A. No. 2:16-cv-02449-KM-JBC (D.N.J.), and *BTG Int’l Ltd.*

v. Glenmark Pharms. Inc., USA, C.A. No. 2:16-cv-05909 (D.N.J). Paper 32, 3.

Patent Owner also states that the '438 patent was the subject of *ex parte* reexamination request No. 90/020,096, but “will not be granted a filing date for failure to comply with the requirements of 37 C.F.R. § 1.501(a).” *Id.* at 2.

B. The '438 Patent

The '438 patent, titled “Methods and Compositions for Treating Cancer,” describes methods that comprise “administering a 17 α -hydroxylase/C_{17,20}-lyase inhibitor, such as abiraterone acetate (i.e., 3 β -acetoxy-17-(3-pyridyl)androsta-5,16-diene), in combination with at least one additional therapeutic agent such as an anti-cancer agent or a steroid.” Ex. 1001, at [54], [57]. As described in the '438 patent, it is believed that testosterone and dihydrotestosterone promote the growth of prostate cancer. *Id.* at 1:49–51. Hormone therapy can be used to suppress the production or block the effects of hormones such as testosterone. *Id.* at 1:43–51.

The enzyme 17 α -hydroxylase/C_{17,20}-lyase (“CYP17”) is involved in testosterone synthesis. *Id.* at 3:66–4:1. CYP17 inhibitors have been shown to be useful in the treatment of cancer, specifically, androgen-dependent disorders like prostate cancer. *Id.* at 5:23–27. Abiraterone acetate, a prodrug of abiraterone, is a CYP17 inhibitor. *Id.* at 2:10–12.

The '438 patent describes administration of a therapeutically effective amount of a CYP17 inhibitor, such as abiraterone acetate, with a therapeutically effective amount of at least one additional therapeutic agent including, but not limited to, an anti-cancer agent, such as mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol,

bicalutamide, or flutamide, or a steroid, such as hydrocortisone, prednisone, or dexamethasone. *Id.* at 2:9–3:20.

C. Challenged Claims

Claim 1 of the '438 patent is reproduced below:

1. A method for the treatment of a prostate cancer in a human comprising administering to said human a therapeutically effective amount of abiraterone acetate or a pharmaceutically acceptable salt thereof and a therapeutically effective amount of prednisone.

Ex. 1001, 16:16–20. Dependent claims 2–20 of the '438 patent describe additional limitations of the method, including the amount of abiraterone acetate and the amount of prednisone used and the type of prostate cancer being treated. *Id.* at 16:21–17:14.

D. Prior Art References Relied Upon by Petitioner

Petitioner relies on the following prior art:

1. Gerber, G.S. & Chodak, G.W., *Prostate specific antigen for assessing response to ketoconazole and prednisone in patients with hormone refractory metastatic prostate cancer*, 144 J. Urol. 1177–79 (1990) (“Gerber”) (Ex. 1004);
2. O'Donnell, A. et al., *Hormonal impact of the 17 α -hydroxylase/C_{17,20}-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer*, 90 British Journal of Cancer 2317–25 (2004) (“O'Donnell”) (Ex. 1005); and
3. Sartor, O. et al., *Effect of prednisone on prostate-specific antigen in patients with hormone-refractory prostate cancer*, 52 Urology 252–256 (1998) (“Sartor”) (Ex. 1006).

E. Instituted Grounds of Unpatentability

We instituted *inter partes* review of claims 1–20 of the ’438 patent on the following grounds:

References	Basis	Claims Challenged
Gerber, O’Donnell, and Sartor	§ 103(a)	1–20

In support of its challenges, Petitioner relies on the declarations of Paul A. Godley, M.D., Ph.D., MPP (Ex. 1002; Ex. 1104; Ex. 1123; Ex. 1129), Robert Stoner, Ph.D. (Ex. 1077; Ex. 1103; Ex. 1122; Ex. 1130), and Ian McKeague, Ph.D. (Ex. 1106). Patent Owner relies on the declarations of Ian Judson, M.D. (Ex. 2028), Matthew Rettig, M.D. (Ex. 2038), Richard Auchus, M.D., Ph.D. (Ex. 2040), and Christopher A. Vellturo, Ph.D. (Ex. 2044).

III. ANALYSIS

A. Claim Interpretation

The Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. *See Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016) (upholding the use of the broadest reasonable interpretation standard); 37 C.F.R. § 42.100(b). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994). Only those terms which are in controversy need to be construed, and only to the extent necessary to resolve the controversy.

See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd., 868 F.3d 1013, 1017 (Fed. Cir. 2017) (“we need only construe terms ‘that are in controversy, and only to the extent necessary to resolve the controversy’”) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

With respect to claim interpretation, “[u]sually [the specification] is dispositive; it is the single best guide to the meaning of a disputed term.” *In re Abbott Diabetes Care Inc.*, 696 F.3d 1142, 1149 (Fed. Cir. 2012) (citations omitted). “To act as its own lexicographer, a patentee must ‘clearly set forth a definition of the disputed claim term’ other than its plain and ordinary meaning.” *Thorner v. Sony Computer Entm’t Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012) (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)).

Petitioner proposes that we construe the claim terms “treat,” “treating,” “treatment,” and “therapeutically effective amount of prednisone.” Pet. 20–21. Petitioner notes that these claim terms have already been construed in IPR2016-00286,¹ Paper 14, and states that it analyzes the claims under those constructions for the purpose of this proceeding. *Id.* In our Decision on Institution, we applied our claim constructions of “treat,” “treating,” “treatment,” and “therapeutically effective amount of prednisone,” as set forth in IPR2016-00286, to the present case. Dec. 5–7; IPR2016-00286, Paper 14, 5–7. Thus, we construed those terms as follows:

¹ IPR2016-00286 is an earlier-filed case involving the ’438 patent, the same grounds, and the same Patent Owner.

Claim term(s)	Construction
“treat,” “treating,” and “treatment”	include the eradication, removal, modification, management or control of a tumor or primary, regional, or metastatic cancer cells or tissue and the minimization or delay of the spread of cancer Ex. 1001, 3:46–50
“therapeutically effective amount of prednisone”	an amount of prednisone effective for treating prostate cancer

Patent Owner states: “Neither party has disputed the Board’s interpretation of this claim term [‘treat,’ ‘treating’ and ‘treatment’] and [Petitioner] has employed it in its Petition.” PO Resp. 4. Patent Owner further states that “the Board’s construction of ‘treat,’ ‘treating’ and ‘treatment’ should be maintained.” *Id.* at 5.

Patent Owner also submitted a claim construction of the terms “treatment” and “treating” by the district court in a companion litigation. Ex. 2010. The district court, after a lengthy analysis, construed the disputed terms as follows: “*Treatment/treating* means the eradication, removal, modification, management or control of a tumor or primary, regional, or metastatic cancer cells or tissue and the minimization or delay of the spread of cancer.” *Id.* at 30. The district court read out of the definition the term “includes.” *Id.* Although we are not bound by the district court’s reasoning and claim constructions in related proceedings, we do not disregard the determinations of a court interpreting the same claim term in a related patent in a concurrent proceeding. *Power Integrations, Inc. v. Lee*, 797 F.3d 1318, 1326–27 (Fed. Cir. 2015) (“The fact that the board is not generally bound by a previous judicial interpretation of a disputed claim term does not mean, however, that it has no obligation to acknowledge that interpretation or to

assess whether it is consistent with the broadest reasonable construction of the term.”). Thus, although we acknowledge and have considered the district court’s interpretation, we retain our broadest reasonable construction of the terms “treat,” “treatment,” and “treating.”

We see no reason to modify our claim construction positions in light of the record developed at trial, and we maintain our claim constructions from the Decision on Institution for the purposes of this Decision. No other claim terms have been presented to us for construction following institution of trial, and we determine that no other claim terms require express construction.

B. Principles of Law

A claim is unpatentable under 35 U.S.C. § 103² if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). A decision on the ground of obviousness must include “articulated reasoning with some rational underpinning to support the legal conclusion of

² The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”), amended 35 U.S.C. § 103. Because the ’438 patent has an effective filing date before the effective date of the applicable AIA amendments, throughout this Decision we refer to the pre-AIA versions of 35 U.S.C. § 103.

obviousness.” *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). The obviousness analysis “should be made explicit” and it “can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *KSR*, 550 U.S. at 418. We analyze the asserted grounds of unpatentability in accordance with the above-stated principles.

C. Level of Skill in the Art

We adopt Petitioner’s contention that a person of ordinary skill in the art

would be a treating clinician specializing in oncology, typically holding an M.D. degree, with at least five years of experience specializing in medical oncology. Alternatively, a POSA would have an M.D., with at least five years of experience specializing in urology and at least two years of clinical experience. A POSA would have also typically worked as part of a multi-disciplinary team and drawn upon not only his or her own skills, but also taken advantage of certain specialized skills of others in the team, to solve a given problem.

Pet. 3–4 (citations omitted). Patent Owner does not appear to dispute Petitioner’s definition in its Patent Owner Response. *See generally* PO Resp. The level of ordinary skill in the art in this case is further demonstrated by the prior art asserted in the Petition. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

D. Overview of the Prior Art

1. O’Donnell

O’Donnell, which is titled “Hormonal impact of the 17 α -hydroxylase/C_{17,20}-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer,” discloses that treatment of prostate cancer with

abiraterone acetate, at a dose of 500–800 mg, can successfully suppress testosterone levels. Ex. 1005, Abstract. O’Donnell also discloses that ketoconazole, another CYP17 inhibitor, has been evaluated as a possible agent with which to achieve decreased production of adrenal steroids, but that abiraterone acetate was developed as a more selective inhibitor. *Id.* at 2318. O’Donnell further discloses that adrenocortical suppression may require administration of replacement glucocorticoid. *Id.* at Abstract, 2323. O’Donnell states that “[s]ome impact on adrenal reserve was predictable from the steroid synthesis pathway.” *Id.* at 2323. Regarding administration of ketoconazole, O’Donnell states that “it is common practice to administer supplementary hydrocortisone” and that this may prove necessary with abiraterone acetate. *Id.* On the basis of the clinical evidence, O’Donnell reports that the need for concomitant therapy of abiraterone acetate with a glucocorticoid needs to be further investigated. *Id.*

2. *Gerber*

Gerber, which is titled “Prostate Specific Antigen for Assessing Response to Ketoconazole and Prednisone in Patients with Hormone Refractory Metastatic Prostate Cancer,” discloses use of ketoconazole, a known CYP17 enzyme inhibitor and inhibitor of gonadal and adrenocortical steroid synthesis, with prednisone to treat patients with progressive prostate cancer. Ex. 1004, 1177. Gerber provides that patients exhibiting progressively increasing prostate specific antigen (“PSA”) levels, when treated with ketoconazole and prednisone, experienced a decrease in PSA levels. *Id.* at 1178–79. Based on its study, Gerber concludes that “there appears to be a small subgroup of patients with progressive prostate cancer despite hormonal therapy who will derive significant benefit from the

combination of ketoconazole and glucocorticoid replacement therapy.” *Id.* at 1179.

3. *Sartor*

Sartor, which is titled “Effect of Prednisone on Prostate-Specific Antigen in Patients with Hormone-Refractory Prostate Cancer,” discloses a trial in which patients with hormone-refractory progressive prostate cancer, who were not receiving concomitant anticancer therapies, were treated with 10 mg of prednisone orally two times a day. Ex. 1006, Abstract. *Sartor* discloses that administration of prednisone alone, as shown by its results, led to an average decline of 33% in PSA responses after initiating prednisone; a majority of patients had PSA progression-free survival for a matter of months following treatment. *Id.* at 254, Table III. *Sartor* concludes that prednisone “can decrease PSA by more than 50% in approximately one third of patients” and hypothesizes “a dose-responsive relationship between glucocorticoid dose and PSA decline.” *Id.* at Abstract.

E. *Obviousness Analysis*

1. *Petitioner’s Arguments*

Petitioner argues that Gerber teaches co-administering the CYP17 inhibitor ketoconazole with prednisone to treat prostate cancer. Pet. 28–29 (citing Ex. 1004, 1177–79). Petitioner further argues that abiraterone acetate “was known to be a potent and more specific inhibitor of CYP17 than ketoconazole and it effectively reduced testosterone levels” (citing Ex. 1002 ¶ 72) and that O’Donnell discloses administering abiraterone acetate to castrate and non-castrate males (citing Ex. 1005, 2320–21, 2324). *Id.* at 29–30. Petitioner argues that “prednisone was known to treat prostate cancer, as well as to offset the side effects from administering a CYP17 inhibitor, such

as abiraterone acetate and ketoconazole” (citing Ex. 1002 ¶¶ 75–84), and that Sartor “teaches administering 20 mg/day prednisone as a monotherapy in patients with mCRPC” (citing Ex. 1006, 252–54). *Id.* at 31. Petitioner presents a claim chart for claim 1, citing the prior art disclosures that Petitioner alleges teach each element of claim 1. *Id.* at 25–28. Petitioner further argues that one of ordinary skill in the art would have had a reasonable expectation of success in practicing the method of claim 1, because Gerber “teaches methods of treating prostate cancer safely and effectively using the CYP17 inhibitor ketoconazole,” O’Donnell “teaches administering the more selective CYP17 inhibitor abiraterone acetate effectively suppresses testosterone levels—a focus of prostate cancer treatment—in castrate and non-castrate males with prostate cancer,” and Sartor “discloses that mCRPC patients had a significant reduction in PSA levels, *i.e.*, $\geq 50\%$, when administered prednisone as a monotherapy.” *Id.* at 34–35.

Petitioner argues that one of ordinary skill in the art “would have had a reason to modify Gerber’s method of administering ketoconazole to use abiraterone acetate, as taught in O’Donnell” because “abiraterone acetate is a potent and more selective inhibitor of CYP17 than ketoconazole and that abiraterone acetate effectively suppressed testosterone levels in both castrate and non-castrate males.” Pet. 24 (citing Ex. 1002 ¶ 67). Additionally, Petitioner argues, one of ordinary skill in the art “would have had a reason to maintain coadministration of prednisone, as taught in Gerber, because prednisone was known to treat prostate cancer on its own, as demonstrated by Sartor.” *Id.* (citing Ex. 1002 ¶ 68). Petitioner summarizes that one of ordinary skill in the art, reading Gerber, O’Donnell, and Sartor, “would have

had a reason to co-administer a therapeutically effective amount of prednisone with abiraterone acetate because (1) prednisone was known to treat prostate cancer and (2) prednisone would reduce the side effects of mineralocorticoid excess that could result from abiraterone acetate treatment.” *Id.* at 33–34 (citing Ex. 1002 ¶¶ 83–84).

Claims 2–20 each depend directly or indirectly from claim 1. Petitioner contends these dependent claims also are unpatentable under 35 U.S.C. § 103 based on Gerber, O’Donnell, and Sartor. Pet. 36–46.

2. Patent Owner’s Non-Obviousness Arguments

Patent Owner presents a series of arguments directed to the art relied upon in Petitioner’s ground, and arguments related to objective indicia of non-obviousness. PO Resp. 5–69. We address each in turn.

a. Patent Owner’s First Argument – Gerber

Patent Owner argues that, contrary to Petitioner’s assertions regarding the prior art’s teachings about the use of ketoconazole and prednisone, Gerber does not establish that ketoconazole and prednisone was an effective treatment for prostate cancer. PO Resp. 5–6. First, Patent Owner argues that Gerber did not demonstrate to one of ordinary skill in the art that co-administration of ketoconazole and prednisone effectively treats prostate cancer. *Id.* at 6. Patent Owner criticizes Gerber for not being a controlled clinical trial and criticizes Gerber’s methodology as falling short when measured against accepted standards. *Id.* at 7 (citing Ex. 1004, 1178; Ex. 2038 ¶ 86). Second, Patent Owner argues that clinical studies before 2006 taught that ketoconazole and prednisone therapy was not a safe and effective treatment for prostate cancer. *Id.* at 9. By 2006, Patent Owner argues, clinical trials showed that ketoconazole plus replacement

glucocorticoid provided only modest activity and no difference in survival from patients receiving only antiandrogen withdrawal, and did not justify phase 3 evaluation. *Id.*

Petitioner argues that, notwithstanding Patent Owner's attacks on Gerber as not being a controlled clinical trial, Gerber is prior art for all that it teaches, namely, the combination of ketoconazole and prednisone as treating prostate cancer. Reply 3 (citing Ex. 1104 ¶ 8). Petitioner replies that Gerber's methodology is sufficient to demonstrate that ketoconazole used with prednisone to treat prostate cancer has "modest activity," and that the claims require nothing more. *Id.* at 4.

We disagree that Petitioner's arguments and evidence regarding the administration of ketoconazole with prednisone are lacking. Gerber, despite the fact that it was not a controlled clinical trial, nevertheless is a peer-reviewed article published in a reputable journal, indicating that treatment with ketoconazole and prednisone demonstrated some degree of success in a group of patients. Ex. 1004. O'Donnell (2004), which is later in time than Gerber (1990), corroborates that in the clinical use of ketoconazole, it is "common practice" to administer supplementary hydrocortisone. Ex. 1005, 2323. Patent Owner's arguments do not undercut the teachings of Gerber, or Gerber's demonstration that the combination of ketoconazole and prednisone worked for some patients, in which it was reasonably well tolerated, considering the circumstances. Ex. 1002 ¶¶ 61, 71; Ex. 1004, 1079; *see Duramed Pharms., Inc. v. Watson Labs., Inc.*, 413 F. App'x 289, 294 (Fed. Cir. 2011) (a reference is "prior art for all that it discloses, and there is no requirement that a teaching in the prior art be scientifically tested, or even guarantee success"). Gerber reasonably stands for the proposition that

administration of ketoconazole and prednisone is tolerated and effective in a subset of patients, and at the time it was published, indicated some measure of efficacy for certain mCRPC patients.

b. Patent Owner's Second Argument – O'Donnell

Patent Owner argues that O'Donnell does not establish that abiraterone acetate has an anti-cancer effect, or suggest concomitant glucocorticoid replacement therapy. PO Resp. 10. Petitioner replies that O'Donnell teaches abiraterone acetate as a potent, more specific CYP17 inhibitor than ketoconazole, and provides a motivation for maintaining prednisone. Reply 5.

First, Patent Owner argues that O'Donnell was designed to assess the safety of abiraterone acetate, rather than its clinical effectiveness, and that O'Donnell found that “abiraterone acetate was very well tolerated and no serious adverse effects attributable to treatment were recorded” over the 12-day testing period. PO Resp. 10–12 (citing Ex. 1005, 2322). Petitioner replies that O'Donnell assessed abiraterone acetate for “testosterone suppression in castrate and non-castrate men with prostate cancer,” which is a goal of prostate cancer treatment, and gives a person of ordinary skill in the art “more than adequate grounds to rely on O'Donnell's teachings.” Reply 6 (citing Ex. 1002 ¶ 26). We find that O'Donnell's stated purpose of investigating the ability of abiraterone acetate to suppress testosterone in prostate cancer patients would have led one of ordinary skill in the art to rely on O'Donnell's teachings. Ex. 1005, 2317, Abstract. We recognize that the

study conducted in O'Donnell was limited in time and scope, but agree with Petitioner that this does not detract from O'Donnell's teachings.

Second, Patent Owner argues that abiraterone acetate and ketoconazole were known to cause different effects on steroid biosynthesis pathways. PO Resp. 13. Patent Owner emphasizes that ketoconazole "was known to be a *non-selective* steroid synthesis inhibitor" whereas abiraterone acetate "was known to be a *selective* CYP17 inhibitor" that targets only CYP17. *Id.* at 13–15 (citing Ex. 2038 ¶¶ 102, 106–08, Fig. 1; Ex. 1005, 2317–18). Petitioner replies that the differences in the steroid biosynthesis pathway between abiraterone acetate and ketoconazole are "inconsequential and irrelevant," focusing instead on the knowledge that "both ketoconazole and abiraterone were CYP17 inhibitors used for the treatment of prostate cancer, and that abiraterone was known in the art to be a potent, more selective inhibitor of CYP17 than ketoconazole." Reply 6 (citing Ex. 1002 ¶¶ 37–39, 62–65).

Based on the information presented during trial, we understand that ketoconazole and abiraterone acetate do not have identical mechanisms. *See, e.g.,* Ex. 1005, 2318, Figure 1. As noted by both Petitioner and Patent Owner, however, abiraterone acetate and ketoconazole are both CYP17 inhibitors. Pet. 11–13; PO Resp. 13–15. Although Patent Owner urges us to focus on the differences in the mechanisms of operation of ketoconazole and abiraterone acetate (PO Resp. 13–15), we look not only at the differences, but also at the similarities.

The evidence demonstrates that one of ordinary skill would have been aware of the differences and the similarities in the mechanisms, and nevertheless would have compared and analogized between the two. Ex. 1005, 2318, Figure 1; Ex. 1002 ¶ 67. O'Donnell refers to ketoconazole

in its discussion of abiraterone acetate, indicating that teachings regarding ketoconazole administration were a starting point for exploration of abiraterone acetate administration. Ex. 1005, 2318. O'Donnell, after evaluating ketoconazole as an agent, turns to an evaluation of abiraterone acetate as a more selective CYP17 inhibitor, i.e., as an improvement on ketoconazole. Ex. 1005, 2318. After presenting the results from its studies, O'Donnell discusses that, in the clinical use of ketoconazole, "it is common practice to administer supplementary hydrocortisone" and that, therefore, "further studies with abiraterone acetate will be required to ascertain if concomitant therapy with glucocorticoid is required on a continuous basis, at times of physiological stress, if patients become symptomatic or indeed at all." *Id.* at 2323. This statement represents the proposition that one of ordinary skill in the art would use the example of ketoconazole's clinical use to take the next investigative steps with abiraterone acetate. We have not been presented with evidence that dissuades us from taking this statement at face value. Thus, we are persuaded that one of ordinary skill in the art would understand that both ketoconazole and abiraterone are CYP17 inhibitors, albeit with different mechanisms. With this knowledge, and given the teachings of the prior art on administration of ketoconazole and administration of abiraterone acetate, we find that one of ordinary skill in the art would look to the administration of ketoconazole for guidance on how to administer abiraterone acetate.

Third, Patent Owner argues that abiraterone acetate was known to not cause the same side effects as ketoconazole. PO Resp. 16. Patent Owner elaborates that "a skilled person would not have expected abiraterone acetate to cause clinically meaningful reductions in glucocorticoid production, and

thus would not cause the same impact on adrenal functions as ketoconazole.” *Id.* at 16–17 (citing Ex. 2038 ¶ 133). Petitioner replies that Patent Owner carefully admits that a person of ordinary skill in the art would have expected abiraterone acetate to inhibit cortisol production. Reply 7 (citing PO Resp. 16–17). Nevertheless, Petitioner argues, one of ordinary skill “would have sought to keep prednisone when administering abiraterone, expecting a decrease in cortisol due to inhibition of CYP17 by abiraterone.” Reply 7 (citing Ex. 1104 ¶ 20).

Both parties present evidence that, based on their respective mechanisms of action, administration of ketoconazole would inhibit production of cortisol, and administration of abiraterone acetate inhibits at least one of the pathways of cortisol production. Pet. 11–13; Ex. 2038 ¶ 100, Figs. 4–5; Tr. 14:21–16:5; Ex. 1005, 2318. Patent Owner states that abiraterone acetate “does not have the same inhibitory effect on cortisol production as ketoconazole” but appears to agree that abiraterone acetate inhibits cortisol to some degree. PO Resp. 15, 16–17. Petitioner additionally asserts that Dr. Rettig’s figures omit a second pathway by which abiraterone acetate inhibits cortisol production. Reply 6–7 (citing Ex. 2038 ¶ 100, Figs. 4–5); Ex. 1104 ¶ 16. Based on the evidence presented, we agree with Petitioner and find that the action of abiraterone acetate would lead to decreased production of cortisol sufficient to alert one of ordinary skill in the art to the existence of such a decrease.

Fourth, Patent Owner argues that there is no evidence that ketoconazole causes mineralocorticoid excess. PO Resp. 17. Rather, Patent

Owner argues, ketoconazole reduces mineralocorticoid production in patients. *Id.* at 18 (citing Ex. 2038 ¶ 104; Ex. 2040 ¶¶ 37–38, 59).

Fifth, Patent Owner argues that there was no evidence, in 2006, that abiraterone acetate would cause mineralocorticoid excess. *Id.* at 19. More particularly, Patent Owner argues that O'Donnell does not mention mineralocorticoid excess, nor does other prior art. *Id.* at 18–19 (citing Ex. 2038 ¶¶ 161–64).

Petitioner replies that one of ordinary skill in the art “would have predicted that abiraterone drive[s] the production of excess mineralocorticoids.” Reply 8 (citing Ex. 1002 ¶¶ 35, 79–81; Ex. 1104 ¶¶ 33–36). Petitioner further replies that Patent Owner’s witness admitted that corticosterone levels would increase and compensate for the lack of cortisol, and that glucocorticoid supplementation is part of the “cornerstone of therapy” in patients “with congenital 17 α -hydroxylase/17,20-lyase deficiency.” Reply 8–9 (citing Ex. 2040 ¶ 47; Ex. 1089, 79:2–80:22, 91:10–93:10).

Petitioner appears to agree with Patent Owner that ketoconazole does not cause mineralocorticoid excess. Tr. 16:12–15 (“Now you have a second problem with abiraterone that you don’t have with ketoconazole that is solved again with glucocorticoid supplementation like prednisone. And that problem is mineralocorticoid excess.”). However, regarding the production of excess mineralocorticoids with abiraterone acetate, we are persuaded that Petitioner’s evidence demonstrates that one of ordinary skill in the art would have understood the possibility or probability of that outcome. Petitioner has reasonably established that one of ordinary skill in the art would have looked at mineralocorticoid production in the CYP17 inhibition scheme to assess the

possibility of mineralocorticoid imbalance in the administration of abiraterone acetate. *See* Ex. 1002 ¶ 35; Ex. 1104 ¶¶ 33–36. In addition, Petitioner has reasonably established that one of ordinary skill in the art would have analogized to congenital CYP17 deficiency, to assess the possibility of mineralocorticoid excess in patients administered abiraterone acetate. *See* Ex. 1104 ¶¶ 32–33; Ex. 1090, 104–05; Ex. 1089, 91:10–93:10; Reply 8. Even though the analogy is not necessarily perfect or complete, an analogy to the problems arising from a congenital CYP17 deficiency likely would shed light on a CYP17 inhibition in other, non-congenital situations. *Id.* We are not persuaded that the lack of explicit discussion of mineralocorticoid excess in Gerber or O’Donnell would discourage the analogy.

Sixth, Patent Owner argues that O’Donnell establishes no need for glucocorticoid replacement with abiraterone acetate. PO Resp. 20. Patent Owner interprets O’Donnell as reporting “clinical results demonstrating *no need* for glucocorticoid replacement treatment with abiraterone acetate.” *Id.* (citing Ex. 1005, 2323; Ex. 2038 ¶¶ 128–29).

Seventh, Patent Owner argues that O’Donnell cautions against glucocorticoid replacement therapy without a clinical justification. *Id.* at 21. Patent Owner relies on O’Donnell’s statement that the “omission of glucocorticoid replacement when treating with aminoglutethimide and ketoconazole has been shown to be safe and effective” to argue that giving glucocorticoid replacement therapy to prostate cancer patients would have to

be clinically justified. *Id.* at 22 (citing Ex. 1005, 2323; Ex. 2038 ¶¶ 122, 128–29).

Eighth, Patent Owner argues that O’Donnell’s ACTH stimulation test results did not establish a need for glucocorticoid replacement therapy with abiraterone acetate. *Id.* at 23. The Synacthen test results reported in O’Donnell, Patent Owner argues, “do not allow any meaningful conclusions to be drawn.” *Id.* at 24 (citing Ex. 2038 ¶ 120–21; Ex. 2040 ¶¶ 11–14, 27–29, 32–34). Moreover, Patent Owner argues, the O’Donnell authors and contemporaneous publications reach the same conclusion. *Id.* at 25 (citing Ex. 1008, 1245; Ex. 1005, 2324).

Petitioner counters Patent Owner’s position that “O’Donnell establishes no need for glucocorticoid replacement with abiraterone,” arguing that (1) Gerber’s teaching of prednisone co-administration would have led one of ordinary skill in the art to continue co-administration of prednisone with abiraterone acetate; (2) O’Donnell showed patients reporting abnormal ACTH tests; and (3) O’Donnell specifically suggested three options regarding using glucocorticoids with abiraterone. Reply 9–10. Petitioner also replies that O’Donnell’s statement that “further studies with abiraterone acetate will be required” is an acknowledgment that glucocorticoids can and may be used with abiraterone acetate. *Id.* at 10.

We agree with Petitioner’s plain reading of O’Donnell as indicating further investigation of the necessity of co-administration of a glucocorticoid with abiraterone acetate. O’Donnell clearly states that adrenocortical suppression may require administration of replacement glucocorticoid. Ex. 1005, Abstract, 2323. O’Donnell also states that “[s]ome impact on adrenal reserve was predictable from the steroid synthesis pathway.” *Id.*

at 2323. Regarding administration of ketoconazole, O'Donnell states that "it is common practice to administer supplementary hydrocortisone" and that this may prove necessary with abiraterone acetate. *Id.* On the basis of the clinical evidence, O'Donnell reports that the need for concomitant therapy of abiraterone acetate with a glucocorticoid needs to be further investigated. *Id.* We disagree with Patent Owner that O'Donnell establishes that there is no need for glucocorticoid replacement with abiraterone acetate. Based on a plain reading, O'Donnell evaluates the evidence and expresses concerns regarding co-administration of a glucocorticoid with abiraterone acetate; it does not conclude that such co-administration is unnecessary.

Regarding Patent Owner's arguments about the risks of administering glucocorticoids, we are not persuaded that those risks outweigh the positive effects in seriously ill patients with limited life expectancy, such that a person of ordinary skill in the art would have been dissuaded from administering glucocorticoids to a mCRPC patient. We have sufficient evidence before us that the risks of glucocorticoid therapy were known, that the longevity of mCRPC patients was short, that glucocorticoid therapy was reasonably well tolerated in the short term, and that any long-term side effects would have been viewed by one of ordinary skill in the art in light of the same. Pet. 24–25, 33; Reply 8–9, 14 (citing Ex. 1002 ¶ 83; Ex. 1104 ¶¶ 21–22). Thus, we find that one of ordinary skill in the art would not have been dissuaded from administering abiraterone acetate with prednisone, but rather, would have been motivated to co-administer prednisone with abiraterone acetate.

Regarding the interpretation of O'Donnell's Synacthen test, we do not agree that the results "do not allow any meaningful conclusions to be drawn." PO Resp. 24. We are persuaded that one of ordinary skill in the art would

understand the results of this test to be an indicator that something was amiss with the O'Donnell Study C patients' cortisol levels following administration of abiraterone acetate. Results of the Synacthen test led O'Donnell to conclude that further studies were needed to determine whether glucocorticoid replacement would be necessary. Ex. 1005, 2323. We understand Patent Owner's position that the Synacthen test "only measures cortisol production, not total glucocorticoid levels in the body" (PO Resp. 24), but do not perceive that a complete picture of a patient's glucocorticoid production is required for one of ordinary skill in the art to be motivated to explore whether glucocorticoid replacement therapy was necessary. Petitioner's expert opines that O'Donnell's results for the Study C patients were "abnormal" and that one of ordinary skill in the art "would have thought to start the patient on a glucocorticoid such as prednisone as a way to avoid issues that would arise from the cortisol deficiency." Ex. 1104 ¶¶ 29–30 (citing Ex. 1009, 2133); Ex. 1002 ¶¶ 64, 83. We credit this testimony as supporting Petitioner's argument that one of ordinary skill in the art, upon reviewing O'Donnell's Synacthen test results and statement regarding impact on adrenal reserve, would not conclude that they lack any significance; rather, they would conclude that they are significant enough to merit further investigation of administration of abiraterone acetate with glucocorticoids.

c. Patent Owner's Third Argument – Sartor

Patent Owner argues that Sartor does not show that prednisone was known to be effective in treating prostate cancer in 2006. PO Resp. 26. By August 2006, Patent Owner argues, one of ordinary skill in the art "would not have considered glucocorticoids, including prednisone, to be an effective

treatment of prostate cancer, but instead to only have a role in treating certain side effects of other drugs or in managing the patient's symptoms." *Id.* at 27 (citing Ex. 2038 ¶¶ 195–98; Ex. 1002 ¶ 116). Petitioner replies that Patent Owner has not rebutted that Sartor "establishes that prednisone was known to treat prostate cancer before the '438 patent priority date." Reply 10.

First, Patent Owner argues, Sartor did not establish to a skilled person in 2006 that prednisone "treats prostate cancer." PO Resp. 28. Patent Owner relies on contemporaneous publications criticizing Sartor, and on Petitioner's expert, to argue that Sartor is of limited usefulness. *Id.* at 28–29 (citing Ex. 1036, 557; Ex. 2038 ¶ 204; Ex. 2161, 87:7–88:18). Patent Owner also critiques the data within Sartor itself as being "quite poor," and as failing to demonstrate that prednisone provided meaningful effects in prostate cancer treatment. *Id.* at 29–30 (citing Ex. 2038 ¶ 203; Ex. 2161, 120:20–121:17). Petitioner rebuffs Patent Owner's attacks on Sartor as being a "retrospective" chart review study," replying that Patent Owner's presents no authority requiring that clinical data come from a particular type of trial. Reply 11.

Sartor, like Gerber, is a peer-reviewed article published in a reputable journal. Ex. 1006; Ex. 1004. Despite the fact that Sartor was a chart review, Sartor nevertheless indicates that treatment with prednisone demonstrated some degree of success in a group of patients. Ex. 1006. Patent Owner's arguments do not undercut the teachings of Sartor, or Sartor's demonstration that prednisone worked for some patients, in which it was reasonably well tolerated, considering the circumstances. Ex. 1006, 252, 255–56; *see In re Fritch*, 972 F.2d 1260, 1264–65 (Fed. Cir. 1992) ("It is well settled that a prior art reference is relevant for all that it teaches to those of ordinary skill in the art."). Sartor reasonably stands for the proposition that administration of

prednisone is tolerated and effective in a subset of patients, and at the time it was published, indicated some measure of efficacy for certain mCRPC patients.

Second, Patent Owner argues that by 2006 it was well known that glucocorticoids elicit only transient PSA responses that do not effectively treat prostate cancer. PO Resp. 30. According to the contemporaneous literature, Patent Owner argues, the “modest PSA responses observed in some patients administered glucocorticoids were generally short-lived, inferior to chemotherapy even in managing patients’ symptoms, and had no meaningful clinical effect.” *Id.* (citing Ex. 2038 ¶¶ 205, 209). Petitioner replies that “a decline in PSA, no matter how ‘modest,’ still indicates a positive treatment effect from prednisone,” and Patent Owner’s admission that Sartor shows a “modest” increased survival rate suffices to meet the limitations of the challenged claims. Reply 11 (citing Ex. 1104 ¶¶ 5, 25; Ex. 1002 ¶¶ 76–78). We agree with Petitioner that use of PSA responses as a metric indicates that certain prostate cancer patients demonstrated some positive results following administration of prednisone. Such a response would meet the limitations of the challenged claims, as argued by Petitioner. Moreover, we note that Patent Owner’s unexpected results arguments, below, use PSA levels as the metric by which to measure efficacy of various prostate cancer drug combination. Reply 4 n.2. Thus, Sartor’s focus on PSA responses does not diminish the relevance of its results.

Third, Patent Owner argues that glucocorticoids were given to manage unique side effects of ketoconazole or cytotoxic chemotherapy agents. PO Resp. 32. These side effects stem from ketoconazole’s inhibition of production of all steroids, Patent Owner argues, and nothing in 2006

suggested abiraterone acetate caused such side effects. *Id.* (citing Ex. 2038 ¶¶ 148–49, 198). Petitioner replies that “whether prednisone was administered concurrently with anti-cancer therapies to treat side effects of those therapies is not dispositive of whether prednisone also has prostate cancer ‘treatment’ activity.” Reply 12. We have addressed Patent Owner’s argument that nothing suggested that abiraterone acetate caused the same side effects as ketoconazole in connection with our discussion of the mechanisms of the two compounds, above. Patent Owner also fails to address Petitioner’s position that Sartor would have been combined with Gerber and O’Donnell not only because prednisone would have ameliorated certain side effects, but because prednisone had its own anti-cancer activity.

Fourth, Patent Owner argues that Petitioner’s expert agrees that prednisone was not known to have anti-cancer treatment effects in prostate cancer patients. PO Resp. 33 (citing Ex. 1002 ¶ 116). Patent Owner refers to Dr. Godley’s testimony that no treating physician would prescribe prednisone alone as an anti-cancer agent to a patient with prostate cancer, except for palliative treatment in patients that had progressed on all other available treatments. *Id.* (citing Ex. 1002 ¶ 116). Petitioner replies that Patent Owner mischaracterizes Dr. Godley’s testimony; it should be read as “regardless of whether he would prescribe prednisone ‘alone,’ [Dr. Godley] maintained that prednisone was shown to have anti-prostate-cancer treatment activity.” Reply 12. Having considered Dr. Godley’s testimony, we understand Dr. Godley’s interpretation of Sartor to be consistent with Petitioner’s position regarding Sartor, i.e., that prednisone has its own anti-cancer effect. Ex. 1002 ¶ 116; Ex. 2162, 61:15–62:17. Additionally, Dr. Godley states that prednisone could be prescribed for palliative treatment, which, as we discuss

herein, is a treatment permitted by the language of the claims. Ex. 2162, 66:1–10, 66:17–67:1.

d. Patent Owner’s Fourth Argument

Patent Owner argues that a skilled person would have found no reason to treat prostate cancer patients with abiraterone acetate and prednisone in 2006. PO Resp. 35.

First, Patent Owner argues that docetaxel chemotherapy had become the standard of care by August 2006, and that secondary hormone therapy was disfavored. PO Resp. 36. This, according to Patent Owner, caused researchers in this field to shift their focus to docetaxel-based regimens and other classes of agents. *Id.* (citing Ex. 2031, 231; Ex. 2161 24:2–8).

Petitioner replies that the prior art’s use of docetaxel does not “teach away” because (1) one of ordinary skill in the art would look beyond the currently established standard of care; (2) the art as a whole does not “teach away”; and (3) neither docetaxel nor any other then-existing therapies for prostate cancer would have discouraged one of ordinary skill in the art from considering the teachings of Gerber, O’Donnell, and Sartor. Reply 16–17. Regarding Patent Owner’s argument that research in the field was focused on agents other than secondary hormonal agents, this does not foreclose or teach away from investigation of a compound such as abiraterone acetate for the treatment of prostate cancer. *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004) (explaining “[t]he prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed”). We are not presented with any evidence that criticizes, discredits, or otherwise discourages use of abiraterone acetate. On

the contrary, abiraterone acetate was already patented and described in printed publications by 2006. *See* Ex. 1005; Ex. 1030. Accordingly, we find that one of ordinary skill in the art seeking to improve upon prostate cancer treatment would have reasonably looked to abiraterone acetate.

Second, Patent Owner argues that glucocorticoids, in 2006, were not given to mCRPC patients absent a compelling clinical justification. PO Resp. 38. Patent Owner argues that even low doses of steroids had been shown to cause serious side effects, including osteoporosis, immunosuppression, hypertension, induction of resistance in tumor cells, steroid myopathy, and gastrointestinal toxicity and bleeds, increase in bone and other metastases, and could fuel prostate cancer growth. *Id.* at 38–41. Thus, Patent Owner argues, a skilled person would have avoided continuous administration of glucocorticoids in patients exhibiting a reduction of cortisol production. *Id.* at 40, 42 (citing Ex. 2038 ¶¶ 137, 146). Petitioner argues that, at best, Patent Owner has shown “that the art might reflect some ‘concerns’ about combining prednisone with abiraterone” but that does not mean such use is not warranted, beneficial, or would not have been obvious. Reply 14. Rather, Petitioner argues, all drugs “carry some concerns over side-effects, and those concerns are weighed against the benefits of use.” *Id.* at 17–18 (citing Ex. 1104 ¶ 27). According to Petitioner, the “overwhelming prior art of evidence shows prednisone and other glucocorticoids” routinely being used for prostate cancer treatment. *Id.* at 18.

We have already addressed a version of this argument, above, finding that although glucocorticoids have certain risks, we are not persuaded that those risks outweigh the positive effects in seriously ill patients with limited life expectancy, such that a person of ordinary skill in the art would have

been dissuaded from administering glucocorticoids to a mCRPC patient. We have sufficient evidence before us that the risks of glucocorticoid therapy were known and that glucocorticoids were routinely used for prostate cancer treatment, and are persuaded that one of ordinary skill in the art would have been motivated to co-administer prednisone with abiraterone acetate.

Third, Patent Owner argues, a skilled person would have treated symptoms of mineralocorticoid excess with other drugs. PO Resp. 43. These drugs would have included mineralocorticoid antagonists such as eplerenone, anti-hypertensives, diuretics, and potassium supplements. *Id.* (citing Ex. 2038 ¶¶ 170–71; Ex. 2040 ¶¶ 66–67). Petitioner argues that Patent Owner has not established why a person of ordinary skill in the art would have preferred eplerenone over prednisone. Reply 18–19. The existence of alternative treatments for mineralocorticoid excess, as discussed by Patent Owner, does not persuade us that one of ordinary skill in the art would employ these alternatives to the exclusion of prednisone. We are presented with no persuasive evidence that negates the reasons discussed for combining an abiraterone acetate with prednisone with a reasonable expectation of successfully treating prostate cancer. *In re Fulton*, 391 F.3d at 1200 (stating a reason to combine does not require a finding that such combination is “the preferred, or most desirable, combination”).

e. Patent Owner’s Fifth Argument

Patent Owner argues that a skilled person would have had no reasonable expectation of success in achieving the ’438 patent invention. PO Resp. 45. First, Patent Owner argues, the prior art provided no basis for a skilled person to expect prednisone would treat prostate cancer. *Id.* According to Patent Owner, the evidence in August 2006 shows that a skilled

person would not have expected that prednisone would be effective in treating prostate cancer, but could instead worsen the patient's cancer. *Id.* at 47. Second, Patent Owner argues that the unpredictability of drug combination therapy in prostate cancer further precludes obviousness. *Id.* at 49.

In making this argument, Patent Owner does not contest, but does discuss, our claim constructions of “therapeutically effective amount of prednisone,” as well as “treat,” “treating,” and “treatment.” PO Resp. 45–46. Our construction of “treat,” “treating,” and “treatment” comes directly from the specification: these terms “include the eradication, removal, modification, management or control of a tumor or primary, regional, or metastatic cancer cells or tissue and the minimization or delay of the spread of cancer.” We construed “therapeutically effective amount of prednisone” as “an amount of prednisone effective for treating prostate cancer,” which invokes the term “treating.”

The specification is directed to the administration of abiraterone acetate with “at least one additional therapeutic agent, *such as an anti-cancer agent or a steroid.*” Ex. 1001, 1:10–12 (emphasis added). Therefore, the specification identifies, as therapeutic agents, both anti-cancer agents and steroids (the specification does not explicitly define “therapeutic agent”). The specification explicitly defines “anti-cancer agent” as “any therapeutic agent that directly or indirectly kills cancer cells or directly or indirectly prohibits, stops or reduces the proliferation of cancer cells.” *Id.* at 4:8–16; *see also supra* (construing “anti-cancer agent”). The specification lists many examples of anti-cancer agents. *See, e.g.,* Ex. 1001, 3:17–18 (listing mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin,

seocalcitol, bicalutamide, and flutamide), 7:43–51 (listing hormone ablation agents, anti-androgen agents, differentiating agents, anti-neoplastic agents, kinase inhibitors, anti-metabolite agents, alkylating agents, *antibiotic agents*, immunological agents, interferon-type agents, intercalating agents, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, mitotic inhibitors, matrix metalloprotease inhibitors, genetic therapeutics, and anti-androgens) (emphasis added), 9:53–10:11. Thus, as set forth by the specification, antibiotic agents are one example of anti-cancer agents. *Id.* at 7:46. The specification lists examples of antibiotic agents, and includes in this list dexamethasone, corticosteroids such as hydrocortisone, *prednisone*, and prednisolone. *Id.* at 9:30–46. Therefore, prednisone, as an antibiotic agent, is an anti-cancer agent, according to the specification.

The specification does not explicitly define “steroid.” The specification lists a few examples of steroids, namely, “corticosteroids or glucocorticoids” (*id.* at 10: 16–17), “hydrocortisone, *prednisone*, or dexamethasone” (*id.* at 3:19–20, 10:20–21 (emphasis added)), and “prednisolone” (*id.* at 10:35). In discussing administration of steroids, the specification provides that the “amount of the steroid administered to a mammal having cancer is an amount that is sufficient to *treat* the cancer whether administered *alone* or in combination with a 17 α -hydroxylase/C_{17, 20}-lyase inhibitor.” *Id.* at 10:21–24 (emphasis added).

The specification, therefore, appears to make a distinction between anti-cancer agents, on the one hand, and steroids, on the other hand. They are treated in the specification as two different categories of therapeutic agents. *See id.* at 3:15–20 (“a therapeutically effective amount of at least one

additional anti-cancer agent, such as, but not limited to, mitoxantrone, paclitaxel, docetaxel, leuprolide, goserelin, triptorelin, seocalcitol, bicalutamide, flutamide, or a steroid including, but not limited to, hydrocortisone, prednisone, or dexamethasone.”).

The anti-cancer agent exemplars in the specification have an anti-cancer effect, as that term is defined. The four steroid examples given (dexamethasone, hydrocortisone, prednisone, and prednisolone), which are identified as antibiotic agents and therefore anti-cancer agents, presumably have an anti-cancer effect. However, because steroids are discussed separately from anti-cancer agents in the specification, they are treated differently than anti-cancer agents: the identified steroids are anti-cancer agents, but they also are treated by the specification as a different category of therapeutic agents. Although steroids may have anti-cancer effects, as suggested by the evidence we have before us in the specification and at trial, the specification does not foreclose that they may also have other therapeutic effects. It would make little sense for the specification to identify the four steroid examples given as anti-cancer agents, and then to address them again as steroids, if these four steroid examples did not have an effect apart from an anti-cancer effect.

Treatment, according to the '438 specification, therefore, can include eradication of a tumor, as would be expected of an anti-cancer agent. Treatment, however, need not exclude other effects that may be provided by steroids. Treatment by steroids can also refer to the other treatments that are “included” in the construction of “treat,” “treating,” and “treatment,” such as management or control of a tumor, cancer cells or tissue, and minimization or delay of the spread of cancer. “As a patent law term of art, ‘includes’ means

‘comprising.’” *SanDisk Corp. v. Memorex Products, Inc.*, 415 F.3d 1278, 1284 (Fed. Cir. 2005) (citations omitted). The terms “management” and “control” in the definition also do not foreclose that the terms “treat,” “treatment,” or “treating” may refer to different effects derived from administration of steroids, apart from anti-cancer effects, such as palliative effects.

We construed “therapeutically effective amount of prednisone” as “an amount of prednisone effective for treating prostate cancer.” Thus, because “treating” can “include” a number of actions, prednisone may be used to “treat” prostate cancer, perhaps by an anti-cancer effect, or perhaps by some other mechanism. Thus, we determine that Petitioner has met its burden that the prior art provides a reasonable expectation that prednisone could be used as a therapeutic agent in the treatment of prostate cancer. Moreover, in this case, in which Petitioner relies on Sartor to demonstrate that prednisone has its own anti-cancer effect, we find that prednisone would “treat” prostate cancer under either definition.

Claim 1, which is directed to the administration of abiraterone acetate and prednisone, does not require a particular result. It does require a “therapeutically effective amount” of each component, but as we have discussed above, the claim language does not require any synergistic anti-cancer results. Therefore, Patent Owner’s reasonable expectation of success argument, viewed in light of the language of the challenged claims and the evidence of record, does not convince us that the Petitioner has not established by a preponderance of the evidence a reasonable expectation of achieving the challenged claims.

3. *Objective Indicia of Non-Obviousness*

In its Petition, Petitioner contends that the Patent Owner may try to rely on secondary considerations of non-obviousness. Pet. 46–65. Specifically, the Petition raises arguments related to unexpected results, commercial success, long-felt need, and copying. *Id.*

In its Response, Patent Owner presents arguments directed to objective indicia of nonobviousness. PO Resp. 50–69. Patent Owner argues that the objective indicia of non-obviousness demonstrate: 1) unexpected results; 2) skepticism and the failure of others; 3) the claimed invention has met a long-felt need; and 4) commercial success. PO Resp. 50–68.

In its Reply, Petitioner presents arguments related to unexpected results, skepticism, failure of others, long-felt need, and commercial success. Reply 19–26.

Factual inquiries for an obviousness determination include secondary considerations based on evaluation and crediting of objective evidence of nonobviousness. *Graham*, 383 U.S. at 17. Secondary considerations may include any of the following: long-felt but unsolved needs, failure of others, unexpected results, commercial success, copying, licensing, and praise. *Id.* The totality of the evidence submitted may show that the challenged claims would not have been obvious to one of ordinary skill in the art. *In re Piasecki*, 745 F.2d 1468, 1471–72 (Fed. Cir. 1984). Before we make our final obviousness determination, we must consider the evidence of obviousness anew in light of any evidence of secondary considerations of nonobviousness presented by Patent Owner. *See Graham*, 383 U.S. at 17–18 (“Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the

circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.”); *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1349 (Fed. Cir. 2012) (“This objective evidence must be ‘considered as part of all the evidence, not just when the decisionmaker remains in doubt after reviewing the art.’” (quoting *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538–39 (Fed. Cir. 1983))).

All types of objective evidence of nonobviousness must be shown to have a nexus to the claimed invention. *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (nexus generally); *In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996) (commercial success); *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) (unexpected results); *Rambus Inc. v. Rea*, 731 F.3d 1248, 1256 (Fed. Cir. 2013) (long-felt need). The stronger the showing of nexus, the greater the weight accorded the objective evidence of nonobviousness. *See Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 306 (Fed. Cir. 1985).

a. Unexpected Results

Patent Owner asserts that unexpected results are demonstrated by the Phase I/II study in which abiraterone acetate was administered as a monotherapy and also together with dexamethasone, a glucocorticoid. PO Resp. 51–54. “Remarkably, many patients in this trial began responding again to treatment” when dexamethasone was added to the treatment regimen after a patient stopped responding to abiraterone acetate monotherapy. *Id.* at 52–53. Patent Owner presents a table comparing abiraterone acetate monotherapy to abiraterone acetate administered with dexamethasone (in clinical trial COU-AA-001, from Ex. 1022) and to abiraterone acetate

administered with prednisone (in clinical trial COU-AA-002, from Ex. 1021) to argue that patients given abiraterone acetate with prednisone responded for more than twice as long on average as those given abiraterone acetate alone. *Id.* at 55. Patent Owner adds that, in Phase III trials, patients had a longer time to PSA progression compared to the Phase II abiraterone acetate monotherapy studies, and experienced an overall survival benefit from the combination. *Id.* at 55–56. Patent Owner also discounts Petitioner’s criticisms of the unexpected results as “baseless,” stating that Petitioner’s focus on median PSA to assess the extent of disease in patient populations reveals the weakness of these assertions. *Id.* at 57–58.

In the Petition, Petitioner argues that unexpected results raised during prosecution do not weigh in favor of patentability, because applicants argued unexpected results based on a comparison of abiraterone acetate and prednisone versus prednisone alone. Pet. 48. Petitioner also argues that “both abiraterone acetate and prednisone were both well-known in the prior art before August 25, 2006” and, therefore, Patent Owner’s alleged unexpected results have no nexus to the ’438 patent. *Id.* at 53. In the Reply, Petitioner argues that the Response (1) fails to report the confidence intervals around the median time to PSA progression (“TTPP”) values; (2) demonstrates no difference in median TTPP between patients who received abiraterone acetate alone and those who received an abiraterone-prednisone combination; (3) improperly compares data from patient populations in separate clinical trials; and (4) relies on clinical studies that were not designed to measure any effect of prednisone. Reply 21–22.

Regarding Patent Owner’s comparison of abiraterone acetate monotherapy with abiraterone acetate/dexamethasone therapy, we agree with

Petitioner that “to the extent that [Patent Owner] tries to draw any conclusion between studies that involve a combination with dexamethasone, we respectfully submit that there’s no nexus there” in that “[d]examethasone is not what’s claimed and there’s no nexus to the claims.” Tr. 19:17–20, 20:2–3. Although dexamethasone and prednisone are both glucocorticoids, Patent Owner does not point us to satisfactory evidence as to why the ordinary artisan would consider dexamethasone and prednisone to be interchangeable for the purpose of comparing results. *Cf.* Ex. 2038 ¶ 240 (stating that a person of ordinary skill would “understand the dexamethasone extension study results to be due to a class effect of glucocorticoids” without further citation). Because the claims cover prednisone, and not any other glucocorticoid, the results of the combination of dexamethasone with abiraterone acetate are of limited use, as we are not informed of the similarities or differences of the mechanism of action of those glucocorticoids or how the mechanism leads to the asserted unexpected results.

Moreover, to the extent the table purportedly compares the abiraterone acetate monotherapy to abiraterone acetate administered with prednisone, the table compares the abiraterone acetate monotherapy administered in clinical trial COU-AA-001 with the abiraterone acetate administered with prednisone in clinical trial COU-AA-002, without explaining or accounting for the differences between the two trials. Tr. 20:10–19.

We determine that there is insufficient evidence that the alleged unpredictable and unexpected results of abiraterone acetate and prednisone are objective indicia of nonobviousness of the challenged claims. Patent Owner does not sufficiently tie the allegedly unpredictable and unexpected

result to the administration of abiraterone acetate and prednisone as claimed. Thus, we determine this consideration does not weigh in favor of the patentability of the challenged claims.

b. Skepticism and the Failure of Others

Patent Owner describes the history of abiraterone acetate development as a series of starts and stops. PO Resp. 61–62. The sponsor of the research described in O’Donnell, according to Patent Owner, terminated its clinical development in 1999. *Id.* at 61. No clinical data concerning abiraterone acetate was published until O’Donnell in 2004. *Id.* Other potential therapeutic agents and regimens for prostate cancer were investigated without success. *Id.* at 62.

Petitioner argues that Patent Owner’s evidence demonstrating its predecessor’s efforts to license abiraterone is overshadowed by O’Donnell’s 2004 publication detailing the benefits of abiraterone. Reply 23. Moreover, Petitioner argues, if there were any skepticism, it was to the abiraterone compound itself. *Id.*

“Evidence of industry skepticism weighs in favor of non-obviousness. If industry participants or skilled artisans are skeptical about whether or how a problem could be solved or the workability of the claimed solution, it favors non-obviousness.” *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1335 (Fed. Cir. 2016).

Based on Patent Owner’s evidence, it does appear that abiraterone acetate was viewed with some skepticism until the application for the ’438 patent was filed in 2006. However, abiraterone acetate was also previously

patented in 1997³ and, therefore, at least some in the industry had overcome their skepticism sufficiently to undertake research on and to seek a patent on the invention of abiraterone acetate alone. Moreover, the claims at issue are directed to the combination of abiraterone acetate with prednisone, whereas Patent Owner's arguments are directed to the purported skepticism of the industry toward abiraterone acetate alone, which falls short of establishing a nexus between skepticism of the industry and the challenged claims. Finally, the "failure of others" argument as it relates to the combination of abiraterone acetate with prednisone may have come about as a result of other factors, such as a blocking patent (Barrie), as we discuss more fully below. Thus, we determine that these factors do not weigh in favor of patentability of the challenged claims.

c. Long-Felt Need

According to Patent Owner, prior to the invention claimed in the '438 patent, "prognosis for men with mCRPC was dismal," and thus, "there was an urgent need for new treatments that would improve survival." PO Resp. 63.

In the Petition, Petitioner argues that there is no showing of long-felt and unmet need or failure of others because (1) "administering abiraterone acetate and prednisone both individually for treating prostate cancer was well-known in the art by August 25, 2006"; (2) "co-administering abiraterone acetate and prednisone did not provide any unexpectedly superior results for treating prostate cancer"; (3) "co-administering prednisone with abiraterone acetate did not satisfy any need to make abiraterone acetate significantly

³ U.S. Patent No. 5,604,213 to Barrie, issued February 18, 1997 ("Barrie") (Ex. 1030).

more effective in prolonging progression-free survival”; and (4) prednisone had long been the standard of care in prostate cancer treatment and prednisone had already been administered with another CYP17 inhibitor, ketoconazole.” Pet. 64–65. In the Reply, Petitioner reiterates these points. Reply 23–24.

We determine that, although drugs that contribute to increasing cancer patient survival rates nearly always satisfy a long-felt need, Patent Owner has not presented sufficient evidence that a specific long-felt need existed for the method of administering abiraterone acetate and prednisone claimed in the ’438 patent. Abiraterone acetate’s availability (and underutilization) for approximately a decade prior to issuance of the ’438 patent undermines Patent Owner’s argument that a long-felt need existed for any regimen based on abiraterone acetate. The record also indicates that, although there were drawbacks to the existing drugs, there were other drugs on the market that were available to prostate cancer patients. Ex. 1002 ¶¶ 28–29; Ex. 2038 ¶ 60. We are not satisfied that long-felt need is necessarily objective indicia of nonobviousness of the challenged claims. Thus, we determine this consideration is neutral regarding the patentability of the challenged claims.

d. Commercial Success

Patent Owner argues that “ZYTIGA[®]-based therapy has been an outstanding commercial success, with U.S. sales reaching \$1.07 billion in 2015 alone and \$1.09 billion in 2016.” PO Resp. 64. Patent Owner further argues that, under any definition of the relevant market, Zytiga’s “combination therapy has achieved substantial market share, demonstrating it enjoys significant commercial success.” *Id.* at 64–65. To support its argument, Patent Owner presents evidence of market share. *Id.* at 65 (citing

Ex. 1012, 6–8; Ex. 2044 ¶¶ 8–9, 64–68, Appendix C, C-1, D; Ex. 2134).

Patent Owner also presents evidence that there is a nexus between the '438 patent claims and the commercial success of Zytiga-based therapy. *Id.* at 66 (citing Ex. 2038 ¶¶ 253–54, 258; Ex. 2044 ¶ 62). Patent Owner also argues that any blocking patent argument is flawed, in that Barrie was available for licensing between 2000 and 2004. *Id.* at 68–69.

In its Petition, Petitioner argues that the existence of a blocking patent (Barrie) and of FDA-based exclusivity limits the applicability of any evidence of commercial success to overcome a *prima facie* case of obviousness. Pet. 55 (citing *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1376–77 (Fed. Cir. 2005)). In discussing Patent Owner's licensing history of the abiraterone acetate patent, Petitioner argues that (1) Patent Owner's argument that only the drug was licensed does not rebut the "blocking patent" activity of Barrie; (2) Patent Owner does not elaborate as to whether the license was exclusive or non-exclusive; (3) Patent Owner does not support its assertion that the licensed party failed to arrive at the '438 patent claims or that abiraterone was available for licensing. *Id.* at 58. Petitioner also disputes that there is any nexus between the Zytiga sales and the '438 patent. *Id.* at 60. More particularly, Petitioner argues that (1) the '438 patent cannot claim invention of the abiraterone or prednisone compounds themselves; (2) both abiraterone and prednisone were well-known in the prior art, as was administering prednisone with other anti-cancer agents, including CYP17 inhibitors; and (3) the lack of evidence that Zytiga's sales are driven by the benefits of adding prednisone to the treatment of abiraterone acetate. *Id.* at 60 (citing Ex. 1077 ¶¶ 33–35). Finally, Petitioner argues that Xtandi has taken Zytiga's market share, and the

prosecution history’s evidence of commercial success is flawed. *Id.* at 62–64. In its Reply, Petitioner does not materially dispute the \$1.07 billion or \$ 1.09 billion annually in sales figures. Petitioner recaps other arguments from its Petition, namely, failure to demonstrate nexus, that Zytiga’s sales were driven by non-patented factors, loss of Zytiga’s market share to Xtandi, Patent Owner’s exclusive focus on marketing expenses, and the blocking patent argument. Reply 24–26.

“When a patentee can demonstrate commercial success, usually shown by significant sales in a relevant market, and that the successful product is the invention disclosed and claimed in the patent, it is presumed that the commercial success is due to the patented invention.” *J.T. Eaton & Co. v. Atl. Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997); *WBIP*, 829 F.3d at 1329. That presumption of nexus, however, is rebuttable, as “a patent challenger may respond by presenting evidence that shows the proffered objective evidence was ‘due to extraneous factors other than the patented invention.’” *WBIP*, 829 F.3d at 1329 (quoting *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1393 (Fed. Cir. 1988)).

There is no real dispute that Zytiga is commercially successful in terms of dollar figures. PO Resp. 64. However, as discussed herein, abiraterone acetate was previously known and patented. Ex. 1030. “Where ‘market entry by others was precluded [due to blocking patents], the inference of non-obviousness of [the asserted claims], from evidence of commercial success, is weak.’” *Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 740 (Fed. Cir. 2013) (quoting *Merck & Co.*, 395 F.3d at 1377). Even if the Barrie patent were available for licensing and was actively shopped around to other companies during 2000 (after which a previous license expired) and 2004

(when the predecessor of Patent Owner took a license), the record evidence does not indicate that those efforts in this span of time remove the deterrent effect of the blocking patent. PO Resp. 68–69 (citing Ex. 2044 ¶¶ 30–33); Reply 23 (citing Ex. 1103 ¶¶ 21–26, 44); Tr. 44:1–14. Thus, although the revenues generated by Zytiga are substantial, the commercial success of Zytiga is mitigated by the existence of a blocking patent. We are persuaded, rather, by Petitioner’s argument that the blocking patent would have deterred others from exploring the commercial potential of abiraterone acetate, and thus, that blocking patent to abiraterone acetate limits the applicability of other evidence of commercial success.

We also note Petitioner’s argument that there is no nexus between the commercial success and the claimed invention, in that the record evidence attributes Zytiga’s commercial success to abiraterone acetate, rather than to the combination of abiraterone acetate and prednisone. Reply 24–25. In this case, if the feature that created the commercial success was known in the prior art, i.e. abiraterone acetate, the success is not pertinent to the issue of obviousness. *Galderma Labs.*, 737 F.3d at 740. As the Zytiga prescribing information indicates, the stated purpose of co-administration of prednisone or “a corticosteroid” is reducing the incidence of adverse reactions due to CYP17 inhibition. Ex. 1052, 3–6 (“[c]o-administration of a corticosteroid” suppresses ACTH drive, resulting in a reduction in the incidence and severity of adverse reactions such as hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition); Ex. 1062, 2–3 (co-administration of a corticosteroid suppresses the ACTH drive, reducing the incidence and severity of mineralocorticoid adverse reactions). This literature’s discussion acknowledges the previously-

known roles of abiraterone acetate and prednisone, and the discussion of a corticosteroid generally contradicts the specific anti-cancer role of prednisone argued by Patent Owner. We are unpersuaded that there is a nexus between the commercial method, namely, the administration of abiraterone acetate and prednisone, and any novel features of the claimed method. Petitioner has demonstrated that both abiraterone acetate and prednisone were known in the prior art. Patent Owner's assertions that the combination of these features drove Patent Owner's increased sales do not demonstrate a nexus between any commercial success and the claimed invention of the '438 patent.

Thus, on this record, it is not clear whether the sales of Zytiga are due to the method recited in the '438 patent, or the known and patented abiraterone acetate itself. Consequently, we cannot conclude from the evidence before us that the commercial success of Zytiga was due to the merits of the invention recited in the claims of the '438 patent. Accordingly, we determine that Petitioner presents sufficient evidence to rebut the presumption of nexus between the commercial success of Zytiga and the claimed method. We, therefore, are not persuaded that Patent Owner's evidence of commercial success supports the nonobviousness of the challenged claims.

4. Summary

As detailed above, the secondary considerations of nonobviousness raised by Patent Owner are neutral or not in favor of the patentability of the challenged claims, and do not outweigh the other *Graham* factors in our obviousness analysis. We determine, therefore, that Petitioner has demonstrated that the preponderance of the evidence of record supports that it would have been obvious to the ordinary artisan at the time of invention to

combine Gerber, O'Donnell, and Sartor with a reasonable expectation of success of achieving the method of challenged claim 1. We also have considered Petitioner's arguments and evidence as to dependent claims 2–20, which reasoning we adopt as our own. We are persuaded, based on those arguments, that Petitioner has demonstrated by a preponderance of the evidence that those claims would have been obvious based on the combination of Gerber, O'Donnell, and Sartor. *See* Pet. 36–46; Ex. 1002 ¶¶ 87–105.

F. Motion to Exclude

Patent Owner filed a Motion to Exclude (Paper 63), to which Petitioner responded (Paper 66) and to which Patent Owner filed a Reply (Paper 70). The party moving to exclude evidence bears the burden of proof to establish that it is entitled to the relief requested, e.g., that the material sought to be excluded is inadmissible under the Federal Rules of Evidence. *See* 37 C.F.R. §§ 42.20(c), 42.62(a).

Patent Owner seeks to exclude Exhibits 1002 ¶¶ 46–57, 106, 117, and 119–23; 1013; 1034; 1048–76; 1077, including but not limited to, ¶¶ 13–22, 24–32, and 72; 1078, 1080; 1082; 1084; 1086; 1087; 1093; 1094; 1100; 1102; 1103 ¶¶ 5–10, 12, 15–19, 27–30, 37, 39–41, and 43; 1104 ¶¶ 3–4, 6–7, 9–13, 15, 17–19, 28, 31, 37–38, 40, 42, 44, 46, and 48; 1106 ¶¶ 17–33, 36, 38–41, 43–49, 51–53, and 56–61; 1107–14; and 1116–19. Paper 63, 15. Patent Owner seeks to exclude these exhibits as (a) expert declarations and exhibits that Patent Owner alleges are outside of the scope of the prior art permitted by 35 U.S.C. § 311(b); (b) sections of Petitioner's declarations and related exhibits that are not cited in the papers, and therefore irrelevant and

prejudicial; and (c) exhibits that lack authenticity or violate the hearsay rule.
Id. at 2.

Petitioner responds that (a) Exhibits 1077, 1048–76, 1078 and 1078 are relevant; (b) portions of Exhibits 1002, 1077, 1103, and 1104 along with Exhibits 1013, 1048, 1050, 1051, 1053–55, 1059, 1066, 1067, 1073–76, 1080, 1082, 1084, 1086, 1093, 1094, 1107–14, and 1116–19 are relevant; (c) Exhibits 1050, 1063, 1065, 1066, 1069, 1074, 1087, 1094, 1100, 1102, 1109, 1112, and 1116, 1034, 1057, 1060–61, 1067, 1068, 1070–73, 1080, 1114, 1119, and Attachments B-1 and B-2 of Exhibit 1077 have been authenticated; and (d) Exhibits 1057, 1060–61, 1065, 1067–73, 1080, 1087, 1100, 1102, and 1109 are not hearsay. Paper 66, 1–12.

Because we do not expressly rely upon Exhibits 1013; 1034; 1048–51, 1053–61, 1063–76; 1078, 1080; 1082; 1084; 1086; 1087; 1093; 1094; 1100; 1102; 1106 ¶¶ 17–33, 36, 38–41, 43–49, 51–53, and 56–61; 1107–14; and 1116–19 in this Decision, Patent Owner’s Motion to Exclude need not be decided as to these exhibits. Accordingly, Patent Owner’s Motion to Exclude is dismissed as moot as to these Exhibits. Below, we address concerns regarding Exhibits 1002, 1052, 1062, 1077, 1103, and 1104.

We disagree that Exhibits 1052 and 1062, upon which Dr. Stoner relies in his declaration, should be excluded. We do not construe Petitioner’s preliminary arguments concerning secondary considerations to be a ground on which this proceeding is based. 35 U.S.C. § 311(b). We credit Petitioner’s argument that Patent Owner “itself attempted to claim commercial success as an objective indicia of non-obviousness in its Patent Owner’s Response.” Paper 66, 2. We find that Exhibits 1052 and 1062 are properly part of the record.

Regarding the portions of Exhibit 1002, 1077, 1103, and 1104 that were not specifically cited in Petitioner's reply, we disagree with Patent Owner that we should exclude these portions. In our proceedings, "[e]vidence consists of affidavits, transcripts of depositions, documents, and things. All evidence must be filed in the form of an exhibit." 37 C.F.R. § 42.63(a). An exhibit "must be filed with the first document in which it is cited." 37 C.F.R. § 42.6(c). The Petition, as filed, references Exhibit 1002 in its List of Exhibits. Pet. i. The Exhibit List (Paper 53) filed with the Reply (Paper 54) references Exhibits 1077, 1103, and 1104. Paper 53, 11. Exhibits 1077, 1103, and 1104 were filed along with the Reply. We find the references to Exhibits 1077, 1103, and 1104 adequate to support the "cited" requirement in 37 C.F.R. § 42.6(c). We are unaware of any legal basis for striking uncited paragraphs of an expert declaration. Thus, the portions of Exhibits 1077, 1103, and 1104 sought to be excluded are not inadmissible, and we shall not exclude them as such.

Accordingly, Patent Owner's Motion to Exclude is *denied* as to Exhibits 1002 ¶¶ 46–57, 106, 117, and 119–23; 1052, 1062, 1077, including but not limited to, ¶¶ 13–22, 24–32, and 72; 1103 ¶¶ 5–10, 12, 15–19, 27–30, 37, 39–41, and 43; and 1104 ¶¶ 3–4, 6–7, 9–13, 15, 17–19, 28, 31, 37–38, 40, 42, 44, 46, and 48, and *dismissed* as to Exhibits 1013; 1034; 1048–51, 1053–61, 1063–76; 1078, 1080; 1082; 1084; 1086; 1087; 1093; 1094; 1100; 1102; 1106 ¶¶ 17–33, 36, 38–41, 43–49, 51–53, and 56–61; 1107–14; and 1116–19.

G. Motions to Seal

Patent Owner filed a motion to seal the confidential versions of the Patent Owner Preliminary Response, as well as Exhibits 2002 and 2003. Paper 11. Patent Owner represents that the parties agreed to a modified

version of the Board's Default Protective Order, submitted as Exhibit 2006, and submitted a redline of the Standing Protective Order as Exhibit 2007. *Id.* at 2. Patent Owner filed another Motion to Seal the confidential version of its Surreply to Patent Owner Preliminary Response. Paper 25. Finally, Patent Owner filed a motion to seal the confidential version of the Declaration of Dr. Vellturo (Exhibit 2044) and the deposition transcript of Dr. Godley (Exhibit 2161), as well as Exhibits 2092, 2093, and 2118. Paper 41.

Petitioner filed a Motion to Seal (Paper 52), moving to seal the confidential version of the Declaration of Dr. Auchus (Exhibit 1089) and the confidential version of the Second Declaration of Dr. Stoner (Exhibit 1103).

The motions to seal are *granted* and the modified protective order *entered*.

There is an expectation that information will be made public where the information is identified in a final written decision, and that confidential information that is subject to a protective order ordinarily would become public 45 days after final judgment in a trial, unless a motion to expunge is granted. 37 C.F.R. § 42.56; Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,761 (Aug. 14, 2012). In rendering this Final Written Decision, it was not necessary to identify, nor discuss in detail, any confidential information. However, a party who is dissatisfied with this Final Written Decision may appeal the Decision pursuant to 35 U.S.C. § 141(c), and has 63 days after the date of this Decision to file a notice of appeal. 37 C.F.R. § 90.3(a). Thus, it remains necessary to maintain the record, as is, until resolution of an appeal, if any.

In view of the foregoing, the confidential documents filed in the instant proceeding will remain under seal, at least until the time period for filing a notice of appeal has expired or, if an appeal is taken, the appeal process has concluded. The record for the instant proceeding will be preserved in its entirety, and the confidential documents will not be expunged or made public, pending appeal. Notwithstanding 37 C.F.R. § 42.56 and the Office Patent Trial Practice Guide, neither a motion to expunge confidential documents nor a motion to maintain these documents under seal is necessary or authorized at this time. *See* 37 C.F.R. § 42.5(b).

H. Conclusion

Having considered the parties' arguments and evidence, we evaluate all of the evidence together to make a final determination of obviousness. *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1075 (Fed. Cir. 2012) (stating that a fact finder must consider all evidence relating to obviousness before finding patent claims invalid). In so doing, we conclude that Petitioner has satisfied its burden of demonstrating, by a preponderance of the evidence, that the subject matter of claims 1–20 would have been obvious over the combination of Gerber, O'Donnell, and Sartor.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–20 are held *unpatentable*;

FURTHER ORDERED that Patent Owner's Motion to Exclude is *denied* as to Exhibits 1002 ¶¶ 46–57, 106, 117, and 119–23; 1052, 1062, 1077, including but not limited to, ¶¶ 13–22, 24–32, and 72; 1103 ¶¶ 5–10, 12, 15–19, 27–30, 37, 39–41, and 43; and 1104 ¶¶ 3–4, 6–7, 9–13, 15, 17–19,

28, 31, 37–38, 40, 42, 44, 46, and 48, and *dismissed* as to Exhibits 1013; 1034; 1048–51, 1053–61, 1063–76; 1078, 1080; 1082; 1084; 1086; 1087; 1093; 1094; 1100; 1102; 1106 ¶¶ 17–33, 36, 38–41, 43–49, 51–53, and 56–61; 1107–14; and 1116–19; and

FURTHER ORDERED, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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