

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN LABORATORIES LIMITED,
Petitioner,

v.

AVENTIS PHARMA S.A.,
Patent Owner.

Case IPR2016-00712
Patent 8,927,592 B2

Before BRIAN P. MURPHY, TINA E. HULSE, and
CHRISTOPHER M. KAISER, *Administrative Patent Judges*.

MURPHY, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Mylan Laboratories Limited (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 1–5 and 7–30 of U.S. Patent No. 8,927,592 (Ex. 1001, “the ’592 patent”). Paper 3 (“Pet.”). Aventis Pharma S.A. (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 7 (“Prelim. Resp.”). We have statutory authority under 35 U.S.C. § 314(a), which provides that an *inter partes* review may not be instituted “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.”

Petitioner challenges claims 1–5 and 7–30 of the ’592 patent as unpatentable under 35 U.S.C. § 103(a). Pet. 13–14. Based on the arguments and evidence presented in the Petition and Preliminary Response, we determine there is a reasonable likelihood Petitioner would prevail with respect to at least one of the claims challenged in the Petition. Therefore, we institute an *inter partes* review.

A. Related Proceedings

Petitioner and Patent Owner identify the following as related district court proceedings in the District of New Jersey regarding the ’592 patent: *Sanofi-Aventis U.S. LLC v. Mylan Laboratories Limited*, C. A. No. 15-03392; *Sanofi-Aventis U.S. LLC v. Apotex Corp*, C. A. No. 15-01835; *Sanofi-Aventis U.S. LLC v. Breckenridge Pharmaceutical, Inc.*, C. A. No. 15-01836; *Sanofi-Aventis U.S. LLC v. Accord Healthcare, Inc.*, C. A. No. 15-02520; *Sanofi-Aventis U.S. LLC v. BPI Labs, LLC*, C. A. No. 15-02521; *Sanofi-Aventis U.S. LLC v. Dr. Reddy Laboratories, Inc.*, C. A. No. 15-02522; *Sanofi-Aventis U.S. LLC v. Glenmark Generics Inc.*, C. A. No. 15-02523; *Sanofi-Aventis U.S. LLC v. Fresenius Kabi USA, LLC*, C. A. No. 15-

02631; *Sanofi-Aventis U.S. LLC v. Actavis LLC*, C. A. No. 15-03107;
Sanofi-Aventis U.S. LLC v. BPI Labs, LLC, C. A. No. 15-02521. Pet. 12;
Paper 6, 2–3.

Petitioner further identifies IPR2016-00627 directed to the compound cabazitaxel, U.S. Patent No. 5,847,170. *Id.* We note that we have denied institution in IPR2016-00627 (Paper 10).

B. Proposed Grounds of Unpatentability

Petitioner advances ten grounds of unpatentability under 35 U.S.C. § 103(a) in relation to the challenged claims in the '592 patent:

Reference[s]	Statutory Basis	Challenged Claims
Winqvist (Ex. 1009) ¹ and TROPIC Listing (Ex. 1008) ²	§ 103	1, 2, 5, 7–9, 12, 13, 17–20, 22–25, 27–29
Winqvist, TROPIC Listing, and Didier (Ex. 1011) ³	§ 103	3, 4
Winqvist, TROPIC Listing, and Mita (Ex. 1012) ⁴	§ 103	7–9

¹ Eric Winqvist et al., *Open clinical uro-oncology trials in Canada*, The Canadian Journal of Urology, 15(1), 3942–49 (February 2008) (“Winqvist”). Ex. 1009.

² Sanofi-Aventis, *XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone Refractory Metastatic Prostate Cancer (TROPIC)*, ClinicalTrials.gov (October 23, 2008) (“TROPIC Listing”). Ex. 1008.

³ U.S. Patent No. 7,241,907 B2 issued July 10, 2007 to Didier et al. (“Didier”). Ex. 1011.

⁴ Alain C. Mita et al., *Phase I and Pharmacokinetic Study of XRP6258 (RPR116258A), a Novel Taxane, Administered as a 1-Hour Infusion Every 3 Weeks in Patients with Advanced Solid Tumors*, Clin. Cancer Res. 2009:15(2), 723–730 (January 15, 2009) (“Mita”). Ex. 1012.

Reference[s]	Statutory Basis	Challenged Claims
Winqvist, TROPIC Listing, and Tannock (Ex. 1013) ⁵	§ 103	10, 11, 14, 16
Winqvist, TROPIC Listing, and Pivot (Ex. 1010) ⁶	§ 103	21, 26, 30
Winqvist, TROPIC Listing, Pivot, and Tannock	§ 103	15
Winqvist and Pivot	§ 103	1, 2, 5, 7–9, 12, 13, 17–30
Winqvist, Pivot, and Didier	§ 103	3, 4
Winqvist, Pivot, and Mita	§ 103	7–9
Winqvist, Pivot, and Tannock	§ 103	10, 11, 14–16

Pet. 13–14. Petitioner supports its challenge with a Declaration by Dr. Rahul Seth (“Seth Declaration”). Ex. 1002.

C. The ’592 Patent

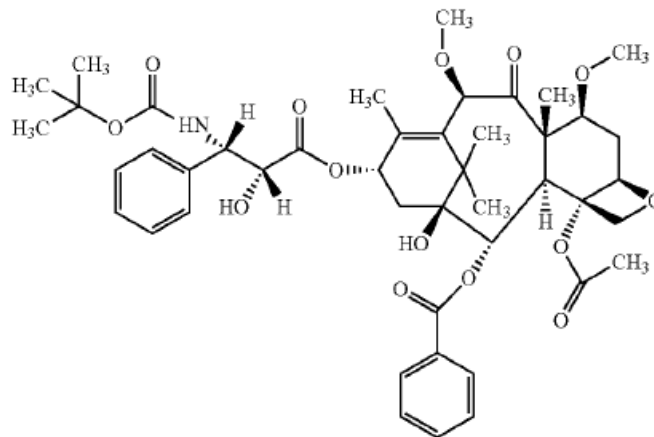
The ’592 patent, titled “Antitumoral Use of Cabazitaxel,” issued January 6, 2015, from an application filed April 26, 2012. Ex. 1001. The ’592 patent claims priority through an international application to a series of provisional applications, the earliest of which is dated October 29, 2009. Ex. 1001, (60), (63). The ’592 patent is directed to the use of cabazitaxel in

⁵ Ian F. Tannock et al., *Docetaxel plus Prednisone or Mitoxantrone plus Prednisone for Advanced Prostate Cancer*, N. Engl. J. Med., 351:15, 1502–1512 (October 7, 2004) (“Tannock”). Ex. 1013.

⁶ X. Pivot et al., *A multicenter phase II study of XRP6258 administered as a 1-h i.v. infusion every 3 weeks in taxane-resistant metastatic breast cancer patients*, Annals of Oncology, 19, 1547–1552 (April 23, 2008) (“Pivot”). Ex. 1010.

the treatment of prostate cancer, particularly metastatic castration resistant prostate cancer (“mCRPC”). *Id.* at 1:19–26. Because cancer cells may develop resistance to docetaxel (Taxotere®⁷), administering cabazitaxel is intended to treat prostate cancer in patients with advanced metastatic disease that has progressed despite previous treatment with a docetaxel-based regimen. *Id.* at 2:61–67. Cabazitaxel is preferably administered in combination with a corticoid, such as prednisone or prednisolone, at a daily dose of 10 mg orally. *Id.* at 3:2–5.

The chemical name for cabazitaxel is 4 α -acetoxy-2 α -benzoyloxy-5 β , 20-epoxy-1 β -hydroxy-7 β ,10 β -dimethoxy-9-oxo-11-taxen-13 α -yl(2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate. *Id.* at 4:28–31. Cabazitaxel is a taxane compound, the chemical structure of which is shown below:



Id. at 4:8–26. Example 1 of the '592 patent describes a large-scale comparative clinical trial of mCRPC patients, whose disease had progressed during or after docetaxel treatment, being treated with either 25 mg/m² of

⁷ Taxotere® is the brand name for docetaxel. We also refer to “Taxotere” in this Decision.

cabazitaxel or 12 mg/m² mitoxantrone, and 10 mg/day of prednisone. *Id.* at 10:30–48. Patients receiving cabazitaxel and prednisone demonstrated a median overall survival that was 2.4 months longer than those receiving mitoxantrone and prednisone. *Id.* at 11:28–37, 11:45–54. The claimed method is directed to administering an effective amount of cabazitaxel and a corticoid to prostate cancer patients whose disease has progressed in spite of previous docetaxel treatment. *Id.* at 5:33–67, 18:54–58, 20:25–30.

D. Challenged Claims

Petitioner challenges claims 1–5 and 7–30 of the '592 patent. Independent claims 1 and 27 are illustrative and are reproduced below:

1. A method for treating a patient with prostate cancer that has progressed during or after treatment with docetaxel, comprising administering to said patient a dose of 20 to 25 mg/m² of cabazitaxel, or a hydrate or solvate thereof, in combination with a corticoid.

27. A method of increasing the survival of a patient with a castration resistant or hormone refractory, metastatic prostate cancer that has progressed during or after treatment with docetaxel, comprising administering a dose of 20 to 25 mg/m² of cabazitaxel, or hydrate or solvate thereof, to the patient in combination with prednisone or prednisolone.

II. ANALYSIS

A. Claim Construction

We determine that only the following claim terms require express construction for purposes of this Decision. *See, e.g., Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (“[C]laim terms need only be construed ‘to the extent necessary to resolve the controversy.’”) (citation omitted).

1. Claim 1: “A method for treating a patient”

Petitioner argues that the preamble phrase in claim 1, “a method for treating,” is a non-limiting statement of the purpose of the claimed method, or, at most, should be construed as “a method intended to benefit a patient.” Pet. 17–19. Patent Owner opposes, arguing that the preamble is limiting and should be construed to mean “a method that produces a therapeutic effect in a patient.” Prelim. Resp. 15–18. We agree with Petitioner for the reasons expressed below.

“Whether to treat a preamble term as a claim limitation is determined on the facts of each case in light of the claim as a whole and the invention described in the patent.” *Am. Med. Sys., Inc. v. Biolitec, Inc.*, 618 F.3d 1354, 1358 (Fed. Cir. 2010) (internal quotation marks omitted). “Absent clear reliance on the preamble in the prosecution history, or in situations where it is necessary to provide antecedent basis for the body of the claim, the preamble generally is not limiting.” *Symantic Corp. v. Computer Assoc. Int’l, Inc.*, 522 F.3d 1279, 1288 (Fed. Cir. 2008). However, “a preamble limits the invention if it recites essential structure or steps, or if it is necessary to give life, meaning, and vitality to the claim.” *Catalina Mktg. Int’l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) (internal quotation marks omitted). “Conversely, a preamble is not limiting where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention.” *Id.* (internal quotation marks omitted).

Petitioner correctly notes that the phrase “a method for treating” does not provide antecedent basis for a limitation recited in the body of the claim

and is not necessary to give meaning to the recited method steps. Only the portion of the preamble reciting “a patient with prostate cancer that has progressed during or after treatment with docetaxel” provides antecedent basis for the step of administering to “said patient” the recited dosage of cabazitaxel and a corticoid. *See Tom Tom, Inc. v. Adolph*, 790 F.3d 1315, 1323–24 (Fed. Cir. 2015) (portion of preamble that “provides a necessary structure for claim 1 does not necessarily convert the entire preamble into a limitation, particularly one that only states the intended use of the invention.”). Although “a method of treating a patient” expresses the purpose of administering an effective amount of cabazitaxel (20 to 25 mg/m²) and a corticoid to a patient (*see* Prelim. Resp. 16), the quoted language “does not result in a manipulative difference in the steps of the claim” and “does not change those amounts or otherwise limit the claim.” *See Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1375–76 (Fed. Cir. 2001).

As Petitioner points out, not every patient necessarily demonstrates a therapeutic effect from the method of treatment. Pet. 19–20 (citing Ex. 1001, Fig. 1 overall survival rate); Ex. 1001, 16:43–44 (“The primary reason for treatment discontinuation in both groups was disease progression (Table 5.)”). Moreover, the recited method steps “are performed the same way regardless [of] whether or not the patient experiences a [therapeutic effect].” *Bristol-Myers Squibb*, 246 F.3d at 1375. Therefore, neither the claim language nor the description of the claimed invention in the ’592 patent supports construing the “method of treating a patient” portion of the preamble to require producing a therapeutic effect in a patient.

Patent Owner cites to the prosecution history of the '592 patent, particularly patent Applicants' reliance on evidence of therapeutic efficacy to distinguish the claimed invention from the prior art of record, in support of its argument that the "method of treating a patient" portion of the preamble is limiting. Prelim. Resp. 17–18 (citing Ex. 1004, 21, 93, 169–175, 184–85, 286, 2014). Patent Applicants relied on evidence of therapeutic efficacy to argue that the claims were not obvious because i) a person of ordinary skill in the art ("POSA")⁸ would not have had a reasonable expectation of successfully treating prostate cancer patients with cabazitaxel, and ii) the therapeutic efficacy of treating prostate cancer patients with cabazitaxel and prednisone was, in fact, unexpected. Ex. 1004, 146–49, 168–179, 184–85, 285–286, 2013–14. Patent Applicants, however, did not cite to or rely on the preamble language of claim 1 to distinguish the claimed invention from the prior art. *Id.* And the Examiner clearly stated his Reasons for Allowance, which acknowledge patent applicants' arguments and evidence of non-obviousness, i.e., "surprising and unexpected" clinical results. *Id.* at 21, 93. The Examiner's Reasons for Allowance do not reference or implicate the preamble language or necessitate construing the "method of treating a patient" portion of the preamble as a claim limitation.

Therefore, based on the current record, we determine that the preamble phrase "a method for treating a patient" in claim 1 is a non-

⁸ The parties' are in general agreement on the level of skill in the art—an oncologist with experience treating metastatic prostate cancer and related medical training and experience. Pet. 9–10; Prelim. Resp. 11. Any differences are not material to our Decision.

limiting statement of the purpose of the claimed method. At most, the phrase would be construed as “a method intended to benefit a patient.”

2. *Claim 27: “A method of increasing the survival of a patient”*

Petitioner argues that the preamble phrase in claim 27, “[a] method of increasing the survival of [a patient],” is a non-limiting statement of the purpose of the claimed method or, at most, should be construed as “a method intended to increase the survival of a patient.” Pet. 19–20. Patent Owner opposes, arguing that the preamble is limiting and should be construed to mean “a method that prolongs the life of a patient as compared to no treatment or palliative treatment, where that method has been demonstrated to provide a statistically significant increase in overall survival.” Prelim. Resp. 19. We agree with Petitioner for the same reasons expressed above regarding “a method for treating a patient” in claim 1.

Therefore, based on the current record, we determine that the preamble phrase in claim 27, “a method of increasing the survival of a patient,” is a non-limiting statement of the purpose of the claimed method. At most, the phrase would be construed as “a method intended to increase the survival of a patient.”

B. Ground 1: Asserted Obviousness of Claims 1, 2, 5, 7–9, 12, 13, 17–20, 22–25, and 27–29 over Winqvist and the TROPIC Listing

Petitioner asserts that the subject matter of claims 1, 2, 5, 7–9, 12, 13, 17–20, 22–25, and 27–29 of the ’592 patent would have been obvious to a POSA based on the combined teachings of Winqvist and the TROPIC Listing in view of the knowledge of a POSA. Pet. 25–38. Patent Owner opposes. Prelim. Resp. 23–35. We address the parties’ arguments below.

1. Winqvist

Winqvist (Ex. 1009) is a February 2008 disclosure of open, uro-oncology clinical trials in Canada. Ex. 1009, 3942. The format of each entry is the same; a descriptive title of the clinical trial followed by an identification of the trial and the entity coordinating it, the trial design, patient population, sample size, and primary endpoint. *Id.* Winqvist discloses a randomized Phase III clinical trial coordinated by Sanofi-Aventis involving treatment of mCRPC patients previously treated with docetaxel. *Id.* at 3948. Winqvist describes the clinical trial as a “study of XRP-6258 [cabazitaxel] at 25 mg/m² in combination with prednisone every 3 weeks compared to mitoxantrone in combination with prednisone for the treatment of hormone-refractory metastatic prostate cancer previously treated with a Taxotere-containing regimen.” *Id.* The primary endpoint is overall survival. *Id.*

With regard to independent claims 1 and 27 of the '592 patent, Winqvist does not disclose that the prostate cancer “has progressed during or after treatment with docetaxel.” *Id.*; Pet. 25–26.

2. The TROPIC Listing

The TROPIC Listing (Ex. 1008) was published in the ClinicalTrials.gov database of the National Library of Medicine, and it was archived by The Internet Archive on October 23, 2008. Ex. 1026, Exh. A. The TROPIC Listing discloses the same Phase III clinical trial as Winqvist, a “randomized, open-label, multi-center study comparing the safety and efficacy of XRP6258 [cabazitaxel] plus prednisone to mitoxantrone plus prednisone in the treatment of hormone refractory metastatic prostate cancer previously treated with a Taxotere [docetaxel]-containing regimen.” Ex.

1008, 1; Ex. 1002 ¶ 118. The TROPIC Listing discloses that cabazitaxel is to be administered every three weeks. Ex. 1008, 1. Patients must have a “[d]ocumented progression of disease (demonstrating at least one visceral or soft tissue metastatic lesion, including a new lesion) . . . [or] rising PSA levels or appearance of [a] new lesion.” *Id.* at 1–2. The primary objective of the TROPIC clinical trial is overall survival. *Id.* at 1. The TROPIC Listing notes the start date of the clinical trial was December 2006. *Id.* at 2.

With regard to independent claims 1 and 27 in the ’592 patent, the TROPIC Listing does not expressly disclose an administration dose. *Id.*; Pet. 7.

3. *Independent Claims 1 and 27*

A claimed invention is unpatentable if the differences between the claimed subject matter 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 the subject matter pertains. 35 U.S.C. § 103(a). Obviousness under 35 U.S.C. § 103 requires an assessment of (1) the “level of ordinary skill in the pertinent art,” (2) the “scope and content of the prior art,” (3) the “differences between the prior art and the claims at issue,” and (4) “secondary considerations” of nonobviousness such as “commercial success, long-felt but unsolved needs, failure of others, etc.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007) (quoting *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966)). A party who petitions the Board for a determination of obviousness must show that “a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing

so.”” *Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007)). We assess Petitioner’s evidence and argument according to this standard.

Petitioner argues that the TROPIC Listing discloses the only limitation of claims 1 and 27 not expressly disclosed in Winquist, namely that the patient’s prostate cancer “has progressed during or after treatment with docetaxel.” Pet. 26–27 (citing Ex. 1002 ¶¶ 118–119). Patent Owner does not directly contest the assertion in its Preliminary Response, instead relying on its preamble-as-claim-limitation argument that neither Winquist nor the TROPIC Listing provides any data to show that cabazitaxel would have produced a therapeutic effect in patients. Prelim. Resp. 23–24. We have rejected Patent Owner’s proposed preamble claim construction in section II.A, above. Petitioner also provides sufficient evidence to support its assertion that a POSA would have had reason to combine the teachings of Winquist and the TROPIC Listing because the two references disclose the same treatment method being used in the same clinical trial. Pet. 26–27 (citing Ex. 1002 ¶¶ 118–120).

The parties present sharply divergent testimonial and documentary evidence of whether a POSA would have had a reasonable expectation of successfully treating prostate cancer patients (claim 1) and mCRPC patients (claim 27) by administering 25 mg/m² cabazitaxel and a corticoid, the treatment protocol disclosed in Winquist and the TROPIC Listing. Pet. 27–29, 33–34, 52–55 (citing, *inter alia*, Ex. 1002 ¶¶ 66–72, 98, 120–22, 132, 133, 169–170, 221–224; Ex. 1008; Ex. 1009; Ex. 1021; Ex. 1022;); Prelim. Resp. 24–44 (citing, *inter alia*, Ex. 1004, 167–182, 184–190; Ex. 2001

¶¶ 31, 32, 37–40, 42–52, 102–107, 110–114, 116–119, 129–134). For example, Petitioner relies on the disclosure and teachings of Attard,⁹ a review article reporting on a Phase I dosing study for cabazitaxel, for the proposition that “it was known in the art that anticancer activity against docetaxel-resistant, castration-resistant prostate cancer was observed in patients treated with cabazitaxel.” Pet. 27 (citing Ex. 1002 ¶¶ 66–69; Ex. 1021, 74–75). Petitioner further relies on the disclosure and teachings of Beardsley.¹⁰ Beardsley reports on a Phase II clinical trial of cabazitaxel administered to docetaxel-resistant metastatic breast cancer patients, originally reported in Pivot (Ex. 1010), for the proposition that the 14% objective response rate was “known to have motivated a Phase III clinical study of cabazitaxel among metastatic prostate cancer patients.” *Id.* at 28 (citing Ex. 1002 ¶¶ 70–72; Ex. 1022, 163).

Patent Owner contests Petitioner’s reasonable expectation of success arguments and evidence, particularly the teachings of Attard and Beardsley. Patent Owner supports its position with new testimonial evidence from Dr. Alton Oliver Sartor, M.D. *See e.g.* Prelim. Resp. 27–28 (citing Ex. 2001 ¶¶ 31, 32, 37–40, 81–83 regarding Attard), 37–38 (citing Ex. 2001 ¶¶ 108–09 regarding Beardsley).¹¹ For example, Patent Owner relies on Dr. Sartor’s

⁹ Gerhardt Attard et al., *Update on tubulin-binding agents*, *Pathologie Biologie* 54, 72–84 (Elsevier 2006) (“Attard”). Ex. 1021.

¹⁰ Emma K. Beardsley and Kim N. Chi, *Systemic therapy after first-line docetaxel in metastatic castration-resistant prostate cancer*, *Curr. Opin. Support Palliat. Care* 2, 161–66 (Wolters Kluwer Health 2008) (“Beardsley”). Ex. 1022.

¹¹ Patent Owner argues that Petitioner has not persuasively addressed Dr. Sartor’s prosecution declaration under 37 C.F.R. § 1.132, in support of Patent Owner’s assertion that the Phase III clinical results in Example 1 of

Declaration testimony for the proposition that “a therapeutic benefit was unpredictable because of the heterogeneity of the disease and the complexity of resistance to both hormone therapy and docetaxel therapy.” *Id.* at 28 (citing Ex. 1004, 180–81, 184–87; Ex. 2001 ¶¶ 31–32, 37–40). The parties’ competing testimonial and documentary evidence also bears on the question of whether the TROPIC clinical trial results were “unexpected” and the weight to be given Patent Owner’s objective evidence of nonobviousness.

At this stage of the proceeding, we find the parties have raised disputed issues of material fact regarding the obviousness inquiries of a reasonable expectation of success and unexpected results. Under such circumstances, “a genuine issue of material fact created by such testimonial evidence will be viewed in the light most favorable to the petitioner solely for purposes of deciding whether to institute an *inter partes* review.” 37 C.F.R. § 42.108(c). Therefore, based on the present record, we determine that Petitioner’s arguments and evidence in support of Ground 1 are sufficient to institute an *inter partes* review with respect to claims 1 and 27. The parties will have the opportunity to cross-examine the respective declarants and submit additional evidence during the trial. 81 Fed. Reg. 18,750, 18,755 (third column) (April 1, 2016).

Patent Owner also argues that Petitioner has failed to comply with 37 C.F.R. § 42.104(b)(2), which requires a petitioner to “specify . . . the patents or printed publications relied upon for each ground,” by relying on

the ’592 patent were unpredictable. Prelim. Resp. 28–30. Petitioner, however, cites to Dr. Seth’s Declaration responding directly to Dr. Sartor’s statements regarding unexpected results. Pet. 57 (citing Ex. 1002 ¶¶ 213–15).

background references outside Ground 1. Prelim. Resp. 26. Patent Owner argues that Petitioner improperly attempts to supply missing claim limitations from such background references. *Id.* Patent Owner suggests denial of the Petition for failure to comply with our rules. *Id.*

Contrary to Patent Owner’s argument, Petitioner does not rely on references other than Winqvist and the TROPIC Listing for disclosure of the method steps recited in claims 1 and 27. Pet. 35–36, 38 (claim charts for claims 1 and 27). Petitioner does, however, rely on the teachings of other references, particularly Attard and Beardsley, to support Petitioner’s obviousness assertion that a POSA would have had a reasonable expectation of successfully treating prostate cancer patients (claim 1) and mCRPC patients (claim 27) based on the method steps disclosed in Winqvist and the TROPIC Listing. Pet. 27–29, 33–34, 52–55. Therefore, for clarity, we exercise our discretion to recast Petitioner’s Ground 1 as one of obviousness over Winqvist and the TROPIC Listing in view of Attard and Beardsley. 35 U.S.C. § 314(a); *see SightSound Techs., LLC v. Apple Inc.*, 809 F.3d 1307, 1312–13 (Fed. Cir. 2015) (noting that governing statutory provisions do not limit the Board’s authority to proceed with AIA trial proceedings only on the specific statutory grounds alleged in the petition); *see also In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1273 (Fed. Cir. 2015) (“Nor does the IPR statute expressly limit the Board's authority at the final decision stage to the grounds alleged in the IPR petition.”), *aff'd*, *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2139–2140 (2016) (“[O]ne important congressional objective . . . [is] giving the Patent Office significant power to revisit and revise earlier patent grants.”).

4. *Dependent Claims 7–9*

Claims 7–9 depend from claim 1 and recite pharmacokinetic (“PK”) parameters produced by administration of 20–25 mg/m² of cabazitaxel. Claims 7–9 recite that cabazitaxel is “administered in an amount to provide” either “an AUC of about 991 ng·h/mL (CV 34%)” (claim 7), “an C_{max} of about 226 ng·h/mL (CV 107%)” (claim 8), or “a plasma clearance of 48.5L/h (CV 39%)” (claim 9). Ex. 1001, 19:3–11. Winqvist and the TROPIC Listing do not disclose or reference any pharmacokinetic parameters resulting from the treatment protocol. Petitioner argues that the recited PK parameters “inherently follow as a direct result of administering cabazitaxel at 25 mg/m²” and, therefore, would have been obvious in view of Winqvist’s disclosure of a 25mg/m² dose of cabazitaxel. Pet. 30–31 (citing Ex. 1002 ¶¶ 56, 124).

We agree with Patent Owner that Petitioner’s inherency assertion is not sufficiently supported. Dr. Seth’s conclusions, drawn from a description of PK analysis in the ’592 patent, are not sufficiently explained to satisfy the high standard required for inherency in an obviousness context. The Federal Circuit has cautioned that inherency “must be carefully circumscribed in the context of obviousness,” because, *inter alia*, “[o]bviousness cannot be predicated on what is unknown.” *Par Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1195 (Fed. Cir. 2014) (citing *In re Rijckaert*, 9 F.3d 1531, 1533–34 (Fed. Cir. 1993), and quoting *In re Shetty*, 566 F.2d 81, 86 (C.C.P.A. 1977)). Patent Owner also shows that infusion time impacts C_{max} and AUC, and differences in formulation also may impact the recited PK distribution ranges. Prelim. Resp. 44–45 (citing Ex. 2061, 188 (Col. 1 ¶ 2); Ex. 2094, 674 (Table IV); Ex. 2089, 347). Petitioner and Dr. Seth do not

address how infusion times or formulation may affect PK distribution profiles.

For the reasons given above, we determine Petitioner has not shown a reasonable likelihood of prevailing with respect to the asserted obviousness of claims 7–9 of the '592 patent in Ground 1.

5. Dependent Claims 2, 5, 12, 13, 17–20, 22–25, 28, and 29

Petitioner argues that the remaining dependent claims recite additional limitations that would have been obvious to a POSA based on Winqvist and the TROPIC Listing. Pet. 29–32, 34–38. Petitioner supports its arguments with claim charts containing citations to Winqvist, the TROPIC Listing, and Dr. Seth's Declaration. *Id.* at 36–38. Patent Owner does not address the remaining dependent claims in dispute.

Based on the present record, we determine Petitioner has provided sufficient argument and evidence in support of Ground 1 to institute an *inter partes* review with respect to dependent claims 2, 5, 12, 13, 17–20, 22–25, 28, and 29 of the '592 patent.

6. Conclusion

Based on the present record, we determine Petitioner has provided sufficient argument and evidence in support of Ground 1 to institute an *inter partes* review with respect to claims 1, 2, 5, 12, 13, 17–20, 22–25, and 27–29 of the '592 patent.

C. Ground 2: Asserted Obviousness of Claims 3 and 4 over Winqvist, the TROPIC Listing, and Didier

Claim 3 depends from independent claim 1. Claim 3 recites cabazitaxel “in the form of an acetone solvate.” Ex. 1001, 18:61–62. Claim

4 depends from claim 3 and further recites “the acetone solvate contains between 5% and 8% by weight of acetone.” *Id.* at 18:63–64.

Petitioner acknowledges that Winqvist and the TROPIC Listing do not disclose an acetone solvate form of cabazitaxel. Pet. 38. Petitioner, however, relies on Didier’s teaching of the preparation of an acetone solvate of cabazitaxel, where the “mean value of the content of acetone is 7%.” *Id.* at 38–39 (citing Ex. 1011, 2:39–42). Didier also states that cabazitaxel “exhibits noteworthy anticancer and antileukemic properties.” Ex. 1011, 1:22–23. Petitioner, relying on Dr. Seth’s testimony, argues that a POSA would have had strong reasons to prepare cabazitaxel in solvate form, to “enable the drug’s dissolution into an aqueous solution suitable for intravenous infusion into a patient.” Pet. 39 (citing Ex. 1002 ¶ 142). Dr. Seth references Liu,¹² which teaches that highly lipophilic paclitaxel has to be in soluble form for intravenous (“i.v.”) administration, in support of his opinion. Ex. 1002 ¶¶ 79–80.

Patent Owner challenges Petitioner’s evidence, particularly Liu, as failing to support a motivation to combine the references to select Didier’s acetone solvate form of cabazitaxel for use in the i.v. treatment method disclosed by the combination of Winqvist and the TROPIC Listing. Prelim. Resp. 50–51. Patent Owner argues that Liu does not support Dr. Seth’s opinion because, when the lipophilicity of a drug such as cabazitaxel presents a formulation problem, Liu suggests the use of surfactants and liposomes rather than alteration of the solid state form of the drug compound

¹² Liu, *Water-Insoluble Drug Formulation*, Chapter 15, 525–568 (CRC Press 2000) (“Liu”). Ex. 1025.

(e.g., forming a solvate) to achieve the requisite solubility. *Id.* (citing Ex. 1025, 527; Ex. 2069). Patent Owner further argues that Liu's list of pre-formulation solvents are not suitable for pharmaceutical preparations and do not support Petitioner's asserted motivation to combine.

The parties have once more raised disputed issues of material fact that we view in the light most favorable to Petitioner based on the present record. *See* 37 C.F.R. § 42.108(c). Therefore, at this stage of the proceeding, we determine that Petitioner has provided sufficient argument and evidence in support of Ground 2 to institute an *inter partes* review with respect to claims 3 and 4. The parties will have the opportunity to cross-examine the respective declarants and submit additional evidence during the trial.

D. Ground 3: Asserted Obviousness of Claims 7–9 Over Winquist, the TROPIC Listing, and Mita

In Ground 3, Petitioner argues that the PK limitations of claims 7–9 of the '592 patent would have been obvious to a POSA based on Winquist, the TROPIC Listing, and Mita. Petitioner notes that Mita expressly discloses AUC and C_{\max} concentrations, and a plasma clearance rate, that fall within the ranges recited in the claims. Pet. 40–41 (citing Ex. 1002 ¶¶ 104, 145–148; Ex. 1012, 729). Petitioner argues that the PK distribution ranges recited in claims 7–9 are minor, obvious limitations in view of the prior art. *Id.* Patent Owner does not address the substance of Ground 3 in its Preliminary Response, apart from invoking its arguments regarding claims 1 and 27 in Ground 1. Prelim. Resp. 52.

Based on the present record, we determine Petitioner has provided sufficient argument and evidence in support of Ground 3 to institute an *inter partes* review with respect to claims 7–9 of the '592 patent.

E. Grounds 4–6: Asserted Obviousness of Claims 10, 11, 14–16, 21, 26, and 30

Ground 4 concerns dependent claims 10 and 11, directed to monitoring neutrophil levels in a patient, and dependent claims 14 and 16, directed to specific doses of the corticoid (10 mg/day) or cabazitaxel (25 mg/m²), respectively. Ground 5 concerns dependent claims 21, 26, and 30, directed to a cabazitaxel dose of 20 mg/m². Ground 6 concerns dependent claim 15, directed to a cabazitaxel dose of 20 mg/m². Petitioner supports its assertions of obviousness in Grounds 4–6 with citations to the respective prior art references and Dr. Seth's Declaration. Pet. 41–45 (citing Ex. 1002 ¶¶ 61, 150, 152–154, 157, 158, 160; Ex. 1008, 1; Ex. 1009, 3948; Ex. 1010, 1547, 1548, 1550; Ex. 1013, 1502–1504). Patent Owner does not address the substance of Grounds 4–6 in its Preliminary Response, apart from invoking its arguments regarding claims 1 and 27 in Ground 1. Prelim. Resp. 52.

Based on the present record, we determine Petitioner has provided sufficient argument and evidence in support of Ground 3 to institute an *inter partes* review with respect to claims 10, 11, 14–16, 21, 26, and 30 of the '592 patent.

F. Grounds 7–10

Grounds 7–10 all rely on Winquist and Pivot to support Petitioner's assertions of obviousness over claims 1–5 and 7–30. As stated above, Pivot

is the Phase II breast cancer study on which Beardsley reported and to which Petitioner cites as additional background information in support of Ground 1. Pet. 27, 34. Therefore, in view of our clarification of Ground 1 as one of obviousness over Winqvist and the TROPIC Listing in view of Attard and Beardsley, and given Petitioner's citation to Pivot in further support of Ground 1, we exercise our discretion and decline to institute review based on Grounds 7–10 advanced by Petitioner. 35 U.S.C. § 314(a); 37 C.F.R. § 42.108(a).

III. CONCLUSION

Petitioner has demonstrated a reasonable likelihood of prevailing with respect to claims 1–5 and 7–30 of the '592 patent challenged in this Petition. At this stage of the proceeding, the Board has not made a final determination as to the patentability of the instituted claims. Our final decision will be based on the full record developed during trial.

IV. ORDER

Accordingly, it is

ORDERED that pursuant to 35 U.S.C. § 314, an *inter partes* review of the '592 patent is instituted on the following grounds:

Claims 1, 2, 5, 12, 13, 17–20, 22–25, and 27–29 as obvious over Winqvist and the TROPIC Listing in view of Attard and Beardsley;

Claims 3 and 4 as obvious over Winqvist, the TROPIC Listing, and Didier;

Claims 7–9 as obvious over Winqvist, the TROPIC Listing, and Mita;

Claims 10, 11, 14, and 16 as obvious over Winquist, the TROPIC Listing, and Tannock;

Claims 21, 26, and 30 as obvious over Winquist, the TROPIC Listing, and Pivot; and

Claim 15 as obvious over Winquist, the TROPIC Listing, Pivot, and Tannock;

FURTHER ORDERED that *inter partes* review is commenced on the entry date of this Order, and pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial; and

FURTHER ORDERED that the *inter partes* review is limited to the grounds of unpatentability listed above, and no other grounds of unpatentability are authorized for *inter partes* review.

IPR2016-00712
Patent 8,927,592 B2

For PETITIONER:

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

For PATENT OWNER:

Dominic A. Conde
Whitney L. Meier
FITZPATRICK CELLA HARPER & SCINTO
dconde@fchs.com
wmeier@fchs.com