

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LIQUIDIA TECHNOLOGIES, INC.,
Petitioner,

v.

UNITED THERAPEUTICS CORPORATION,
Patent Owner.

IPR2020-00770
Patent 9,604,901 B2

Before ERICA A. FRANKLIN, ZHENYU YANG, and
JOHN E. SCHNEIDER, *Administrative Patent Judges*.

PER CURIAM

JUDGMENT

Final Written Decision
Determining Some Challenged Claims Unpatentable
35 U.S.C. § 318(a)

Denying Petitioner's Request to Strike
37 C.F.R. § 42.5

Denying Patent Owner's Motion to Exclude
37 C.F.R. § 42.64(c)

Granting Petitioner's Motion to Submit Supplemental Information
37 C.F.R. § 42.123(b)

I. INTRODUCTION

Liquidia Technologies, Inc. (“Petitioner”) filed a Petition (Paper 1 (“Pet.”)), seeking an *inter partes* review of claims 1–9 of U.S. Patent No. 9,604,901 B2 (Ex. 1001, “the ’901 patent”). We instituted trial to review the challenged claims. Paper 7 (“Dec.” or “Decision to Institute”). Thereafter, United Therapeutics Corporation (“Patent Owner”) filed a Response to the Petition (Paper 12, “PO Resp.”), Petitioner filed a Reply (Paper 15), and Patent Owner filed a Sur-reply (Paper 25).

The parties filed a Joint Paper Concerning Petitioner’s Request to Strike Portions of Patent Owner’s Paper Nos. 12 and 25 and Exhibits 2002 and 2025. Paper 29. The parties also briefed the issues of (1) whether we should exclude Exhibits 1002 and 1012 (Papers 31, 32, 37), and (2) whether Petitioner may submit, as supplemental information, the transcript and order from the *Markman* hearing in a parallel district court case (Papers 38, 40). An oral hearing for this proceeding was held on June 23, 2021, and the transcript of that hearing is of record. *See* Paper 44 (“Tr.”).

The Board has jurisdiction under 35 U.S.C. § 6 and issues this final written decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons provided below, we conclude Petitioner has established by a preponderance of the evidence that claims 1–5, 8, and 9 are unpatentable. Petitioner, however, has not established by a preponderance of the evidence that claims 6 and 7 are unpatentable.

A. The '901 Patent

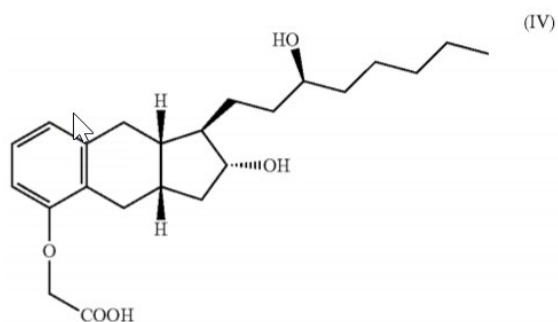
The '901 patent relates to “an improved process to convert benzindene triol to treprostinil via salts of treprostinil and to purify treprostinil.”

Ex. 1001, Abstract.

Prostacyclin derivatives are useful pharmaceutical compounds. *Id.* at 1:23–26. Treprostinil, a known prostacyclin derivative, is the active ingredient in Remodulin. *Id.* at 1:27–32. Before the '901 patent, treprostinil had been prepared as described in Moriarty¹ and other prior-art references. *Id.* According to the '901 patent, because treprostinil is “of great importance from a medicinal point of view, a need exists for an efficient process to synthesize th[is] compound[] on a large scale suitable for commercial production.” *Id.* at 1:66–2:3.

The '901 patent discloses “a process for the preparation of a compound having formula IV, or a hydrate, solvate, or pharmaceutically acceptable salt thereof.” *Id.* at 8:44–46. Petitioner represents that Formula IV is treprostinil. Pet. 11; Ex. 1002 ¶ 30. Formula IV has the following structure:

¹ Moriarty et al., The Intramolecular Asymmetric Pauson-Khand Cyclization as a Novel and General Stereoselective Route to Benzindene Prostacyclins: Synthesis of UT-15 (Treprostinil), 69 J. ORG. CHEM. 1890–1902 (2004) (Ex. 1009). Moriarty is one of the prior-art references asserted in this proceeding.

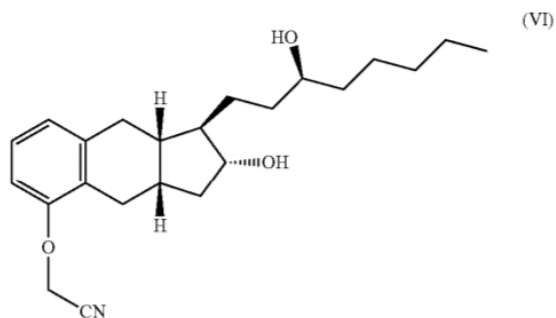
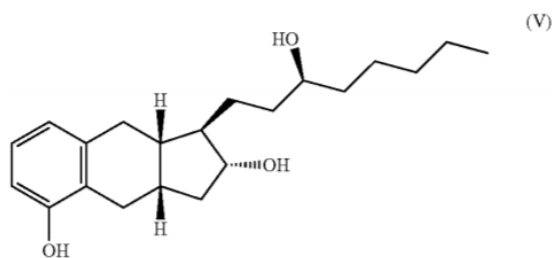


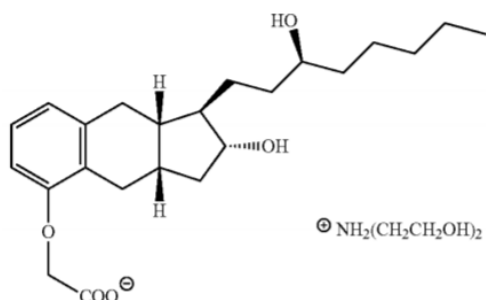
The figure above shows the structure of Formula IV. Ex. 1001,
8:48–63.

The process of the '901 patent comprises

- (a) alkylating a compound of structure V with an alkylating agent such as ClCH₂CN to produce a compound of formula VI,
- (b) hydrolyzing the product of step (a) with a base such as KOH,
- (c) contacting the product of step (b) with a base B such as diethanolamine to form [sic] a salt of the following structure, and
- (d) reacting the salt from step (b) with an acid such as HCl to form the compound of formula IV.

Id. at 8:65–9:48. Structure V, formula VI, and the salt formed in step (c) have the following structures:





The figures above show the structures of structure V, formula VI, and the salt formed in step (c). *Id.* at 9:1–28, 9:33–45. The '901 patent states that “[i]n one embodiment, the purity of compound of formula IV is at least 90.0%, 95.0%, 99.0%, 99.5%.” *Id.* at 9:49–50.

According to the '901 patent:

The quality of treprostinil produced according to this invention is excellent. The purification of benzindene nitrile by column chromatography is eliminated. The impurities carried over from intermediate steps (i.e. alkylation of triol and hydrolysis of benzindene nitrile) are removed during the carbon treatment and the salt formation step. Additional advantages of this process are: (a) crude treprostinil salts can be stored as raw material at ambient temperature and can be converted to treprostinil by simple acidification with diluted hydrochloric acid, and (b) the treprostinil salts can be synthesized from the solution of treprostinil without isolation. This process provides better quality of final product as well as saves significant amount of solvents and manpower in purification of intermediates.

Id. at 16:66–17:12, *see also id.* at 6:4–18 (the same).

B. Illustrative Claim

Claim 1 is the only independent claim. With the Certificate of Correction (Ex. 1006, 2) incorporated, it is reproduced below:

1. A pharmaceutical batch consisting of treprostinil or a salt thereof and impurities resulting from (a) alkylating a benzindene triol, (b) hydrolyzing the product of step (a) to form a solution

comprising treprostinil, (c) contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil, (d) isolating the salt of treprostinil, and (e) optionally reacting the salt of treprostinil with an acid to form treprostinil, and wherein the pharmaceutical batch contains at least 2.9 g of treprostinil or its salt.

C. Instituted Grounds of Unpatentability

We instituted trial to determine whether the challenged claims are unpatentable based on the following grounds:

Claims Challenged	35 U.S.C. § ²	References
1–9	103(a)	Phares ³
1–9	103(a)	Moriarty, Phares

To support their respective arguments, Petitioner relies on the Declaration of Jeffrey D. Winkler, Ph.D. (Exs. 1002, 1017) and Sylvia Hall-Ellis, Ph.D. (Exs. 1015, 1052); and Patent Owner relies on the Declarations of Rodolfo Pinal, Ph.D. (Exs. 2002, 2025).

D. Related Matters

Patent Owner asserted the '901 patent against Petitioner in *United Therapeutics Corporation v. Liquidia Technologies, Inc.*, No. 1:20-cv-00755 (D. Del.) (“the district court case”). Paper 5, 1.

Petitioner filed IPR2020-00769, challenging the claims of U.S. Patent No. 9,593,066 (“the '066 patent”), a patent in the same family as

² The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the '901 patent has an effective filing date prior to March 16, 2013, we apply the pre-AIA version of § 103.

³ PCT Application No. WO 2005/007081 A9, published Jan. 27, 2005 (Ex. 1008).

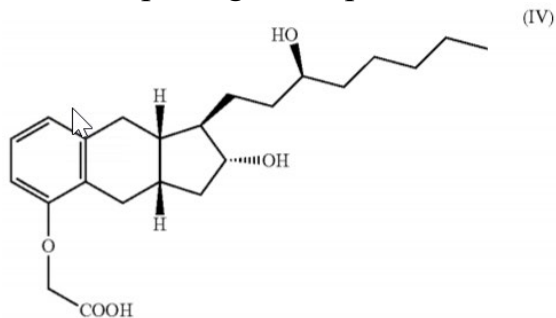
the '901 patent. *Id.* We declined to institute trial in that case.

IPR2020-00769, Paper 7.

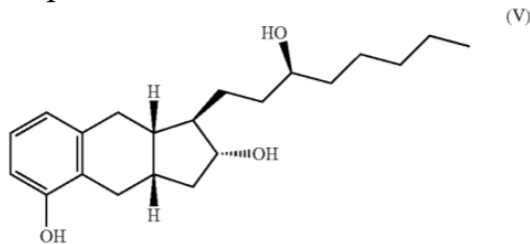
U.S. Patent No. 8,497,393 (Ex. 1004, “the '393 patent”) is a parent of the '901 patent. Ex. 1001, code (63). The '393 patent is the subject of *SteadyMed Ltd. v. United Therapeutics Corp.*, IPR2016-00006 (“the '393 IPR”). The petition for the '393 IPR challenged claims 1–5, 7–9, 11–14, and 16–20 of the '393 patent as anticipated by Phares, and as obvious over Moriarty and Phares. IPR2016-00006, Paper 82 (PTAB March 31, 2017) (“the '393 Decision” or “the '393 Dec.”), 7. It also challenged claims 6, 10, 15, 21, and 22 as obvious over Moriarty, Phares, and additional prior art. *Id.*

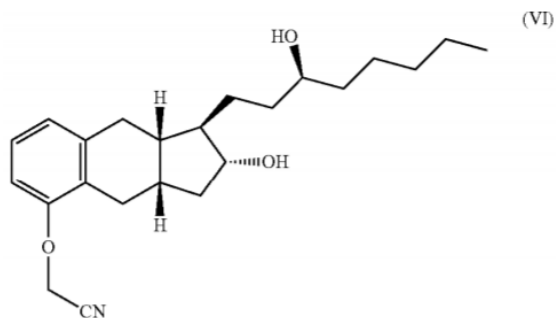
Claim 9 of the '393 patent recites:

9. A product comprising a compound of formula IV

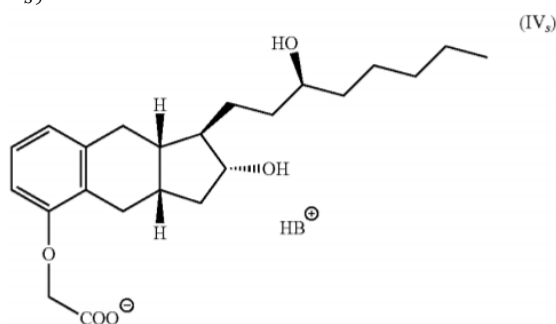


or a pharmaceutically acceptable salt thereof, wherein said product is prepared by a process comprising
(a) alkylating a compound of structure V with an alkylating agent to produce a compound of formula VI,





(b) hydrolyzing the product of formula VI of step (a) with a base,
(c) contacting the product of step [(b)] with a base B to form a salt of formula IV_s, and



(d) optionally reacting the salt formed in step (c) with an acid to form the compound of formula IV.

Formula IV of the '393 patent is the same as that of the '901 patent, and shows the structure of treprostinil. *See* the '393 Dec. 24 (“Claim 9 . . . is drawn to a product comprising the specific treprostinil compound.”).

On March 31, 2017, the '393 IPR panel held that the petitioner in the '393 IPR prevailed in all asserted grounds, and that claims 1–22 of the '393 patent are unpatentable. *Id.* at 44, 67, 84, 90. Specifically, it determined that the petitioner there demonstrated the obviousness of claim 9 over the combination of Moriarty and Phares. *Id.* at 44, 68.

In reaching that conclusion, the '393 IPR panel found that “an ordinarily skilled artisan at the time of invention of the '393 patent would have had a doctorate in chemistry, pharmaceuticals, pharmaceutical sciences,

medicine, or a related discipline, or a lesser degree in one of those fields, with correspondingly more experience.” *Id.* at 49. It also found that the relevant skilled artisan “would have had experience in synthesizing and analyzing complex organic compounds.” *Id.*

Dr. Winkler, Petitioner’s expert in this proceeding, also provided testimony in the ’393 IPR. He testified that “an ordinarily skilled artisan would have sought to combine Moriarty and Phares in order to eliminate the intermediate purification step taught by Moriarty, thereby increasing synthetic efficiency and lowering production costs for treprostinil diethanolamine salt.” *Id.* at 46. The ’393 IPR panel credited this testimony, finding that Phares teaches “intermediate purification is unnecessary to the production of treprostinil diethanolamine salt by the disclosed process.” *Id.* at 47; *see also id.* at 50 (“[T]he proposed combination of Moriarty and Phares would eliminate the need for intermediate purification as required by Moriarty alone, and thereby confer efficiency and cost benefits.”). Thus, it determined that “an ordinarily skilled artisan would have sought to combine Moriarty and Phares in order to reap these efficiency and cost benefits.” *Id.* at 50.

The ’393 IPR panel also found “an ordinarily skilled artisan would have sought to make the proposed combination for the independent reason that Phares is directed to improving treprostinil, and the Moriarty process . . . was a well-known way to make treprostinil.” *Id.* It further found “an ordinarily skilled artisan would have a reasonable expectation of success in combining Moriarty and Phares.” *Id.* at 52. The ’393 IPR panel analyzed the evidence of objective indicia, including long-felt but unmet need and

unexpected results, but found that the evidence did not show nonobvious. *Id.* at 57–67. Thus, it concluded that the combination of Moriarty and Phares renders claim 9 of the '393 patent obvious. *Id.* at 68.

The Federal Circuit affirmed that decision. *United Therapeutics Corp. v. SteadyMed Ltd.*, 702 F. App'x. 990 (Fed. Cir. 2017).

E. The Prosecution of the '901 Patent

During the prosecution of the '901 patent, the applicant submitted the petition for the '393 IPR in an IDS. Ex. 1006, 127. Thereafter, the examiner issued an office action, rejecting then pending claims 1–3, 6, 8, and 9 as anticipated by Moriarty. *Id.* at 118. The examiner found that those claims are product-by-process claims and stated

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from the product of the prior art, the claim is unpatentable even though the prior art product was made by a different process.

Id. at 119 (quoting *In re Thorpe*, 777 F.2d 695, 698 (Fed. Cir. 1985)).

The examiner found that

Moriarty et al disclose[s] a method for preparing treprostinil. Said method comprises the steps of: (a) alkylation of benzindene triol and (b) hydrolysis of the product of step (a) 441 g of treprostinil (a therapeutically effective amount) was prepared at 99.7% purity. Moriarty also discloses removing impurities via extraction and further purification via crystallization. Although the method of Moriarty and the steps recited in the instant claims are not identical, the product obtained is the same.

Id. at 118–19.

The examiner also rejected then pending claims 10–12 as obvious over Moriarty and Phares. *Id.* at 120. The examiner acknowledged that Moriarty fails to teach the “preparation of a diethanolamine salt of treprostinil” and the “preparation of a pharmaceutical product comprising diethanolamine salt.” *Id.* The examiner, however, found “Phares et al teach[es] preparation of treprostinil diethanolamine by dissolving treprostinil acid and treating it with diethanolamine.” *Id.* at 121.

According to the examiner,

One skilled in the art practicing the invention of Phares would have found it obvious to prepare a diethanolamine salt of treprostinil prepared by the method of Moriarty. Moriarty discloses a method for preparing a treprostinil acid which is a needed starting material for the process of Phares. The resulting salt would meet the limitations directed to pharmaceutical product because treprostinil diethanolamine is the sole claimed component of the claimed pharmaceutical product.

One skilled in the art would have found it obvious to prepare a pharmaceutical product from the treprostinil diethanolamine salt of Phares prepared from the treprostinil free acid that has been obtained by the process of Moriarty.

Id.

In response to the rejections, the applicant cancelled then pending claims 2 and 3, and amended other claims. *Id.* at 96–97. Most significantly, the applicant amended claim 1 as follows:

1. (Currently Amended) A pharmaceutical batch comprising consisting of treprostinil or a salt thereof and impurities resulting from ~~prepared by~~ (a) alkylating a benzindene triol, (b) hydrolyzing the product of step (a) to form a solution comprising treprostinil, (c) contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil, (d) isolating the salt of treprostinil, and (e) optionally reacting the

salt of treprostinil with an acid to form treprostinil, and; wherein the pharmaceutical batch contains at least 2.9 g of treprostinil or its salt.

Id. at 96.

The applicant also submitted “Patent Owner’s Response and expert declarations from Dr. Williams and [Dr.] Ruffolo” from the ’393 IPR. *Id.* at 98. Relying on the expert declarations, the applicant argued that “a pharmaceutical batch produced according to steps (a)-(e) of claim 1 is different from the product produced by the process described in Moriarty 2004” because “the processes result in products having different impurity profiles, and in fact, the pharmaceutical batch of claim 1 has higher average purity.” *Id.* at 99. The applicant highlighted that

As noted in the Patent Owner’s [’393] IPR Response, the differences between claim 1’s pharmaceutical batch and a product produced according to the process of Moriarty were significant enough to result in FDA’s acceptance of a new purity specification for the commercial product, thus proving that the products are not the same in the eyes of the FDA.

Id. As a result, the applicant requested that the examiner withdraw the anticipation rejection. *Id.*

Regarding the obviousness rejection, the applicant contended that “the differences in the resulting products, as explained above, would not have been expected based on the prior art.” *Id.* According to the applicant, “it would not have been obvious to use the salt formation step of Phares to decrease amounts of stereoisomer impurities of treprostinil” and an ordinarily skilled artisan “would have had no reasonable expectation of success in removing any undesired treprostinil stereoisomer impurities by salt formation and subsequent regeneration of the free acid.” *Id.* at 99–100.

The applicant again emphasized that “even small changes in impurity are important to FDA.” *Id.* at 100. Thus, according to the applicant, “FDA’s decision to adopt a new purity specification for the resulting product further establishes unobviousness of the presently claimed invention.” *Id.*

Thereafter, the examiner withdrew the anticipation and obviousness rejections “in view of applicants’ arguments, amendments and the accompanying declarations.” *Id.* at 87. And, after the applicant filed a terminal disclaimer to overcome a double-patenting rejection (*id.* at 73–75), the examiner allowed claims 1, 6, and 8–14 (*id.* at 62), and they issued as the challenged claims 1–9. The ’901 patent issued on March 28, 2017, three days before the Board issued the ’393 Decision.

II. ANALYSIS

A. Principles of Law

To prevail in this *inter partes* review, Petitioner “shall have the burden of proving a proposition of unpatentability by a preponderance of the evidence.” 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d) (2019).

A patent claim is unpatentable under 35 U.S.C. § 103(a) 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 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;

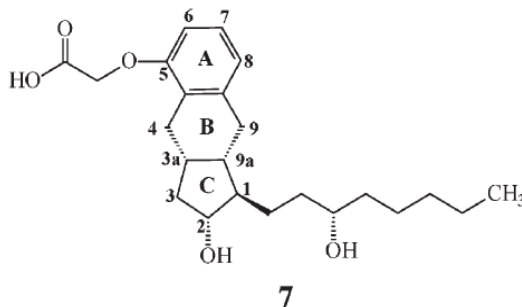
(3) the level of skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *KSR*, 550 U.S. at 406.

We analyze the instituted grounds of unpatentability in accordance with these principles.

B. Prior Art Disclosures

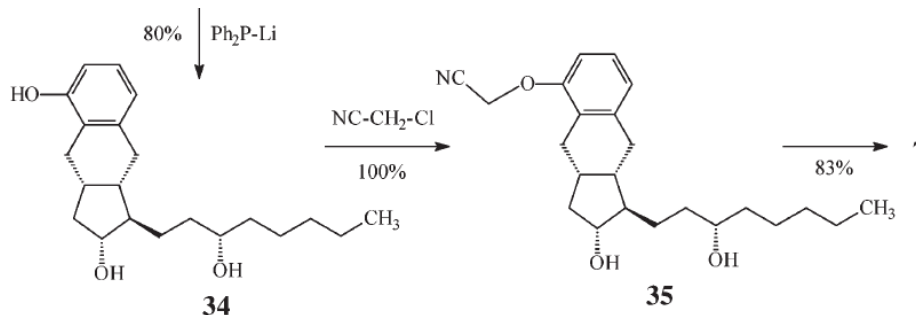
1. Moriarty

Moriarty describes synthesizing treprostinil “via the stereoselective intramolecular Pauson-Khand cyclization.” Ex. 1009, 1.⁴ Formula 7 of Moriarty is reproduced below:



Id. at 3. Formula 7 of Moriarty depicts the chemical structure of treprostinil. *Id.*

An excerpt of Scheme 4 of Moriarty is reproduced below:



⁴ For Moriarty, the parties cite to the pagination added by Petitioner. For consistency, we do the same.

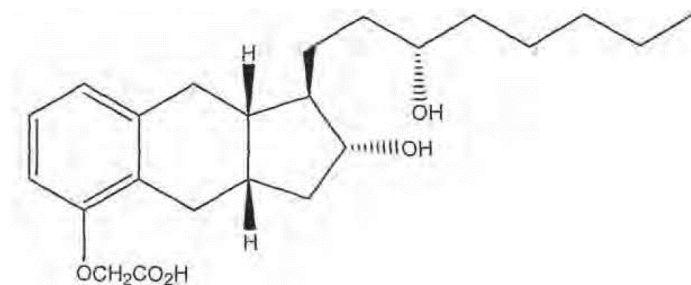
Id. at 6. The excerpted portion of Scheme 4 of Moriarty illustrates that “[t]riol **34** was alkylated at the phenolic hydroxyl group with use of chloroacetonitrile in refluxing acetone with potassium carbonate (**34** → **35**) and nitrile **35** was hydrolyzed with ethanolic potassium hydroxide to yield UT-15 (**7**),” treprostinil. *Id.* at 8.

2. Phares

Phares teaches compounds, including treprostinil and derivatives thereof, “and methods for inducing prostacyclin-like effects in a subject or patient.” Ex. 1008, 8.⁵ “Treprostinil is a chemically stable analog of prostacyclin, and as such is a potent vasodilator and inhibitor of platelet aggregation.” *Id.* Phares states that “[t]he compounds provided herein can be formulated into pharmaceutical formulations and medicaments that are useful in the methods of the invention.” *Id.*; *see also id.* at 48 (“provid[ing] for compositions which may be prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts thereof, with pharmaceutically acceptable carriers, excipients, binders, diluents or the like, to treat or ameliorate a variety of disorders related vasoconstriction and/or platelet aggregation”).

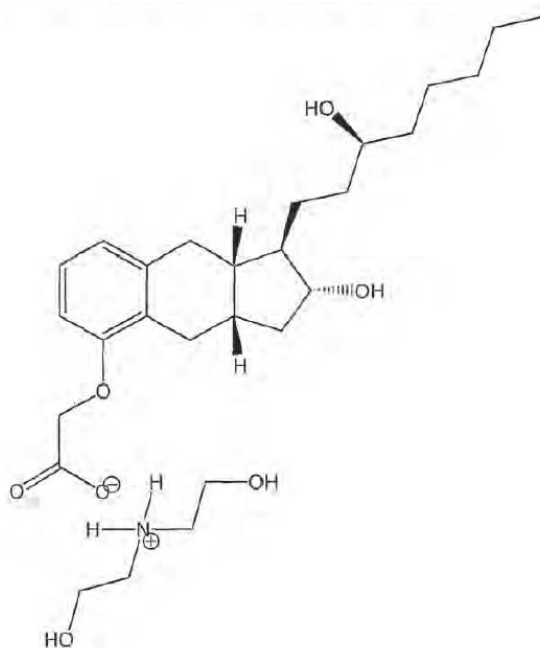
The chemical structure of treprostinil, as shown in Phares, is reproduced below:

⁵ For Phares, the parties cite to the original page numbers of the exhibits, and not the pagination added by Petitioner. For consistency, we do the same.



The figure above shows the structure of treprostinil. *Id.* at 8.

Phares teaches that “[a] preferred embodiment of the present invention is the diethanolamine salt of treprostinil.” *Id.* at 9. The structure of the diethanolamine salt of treprostinil, as shown in Phares, is reproduced below:

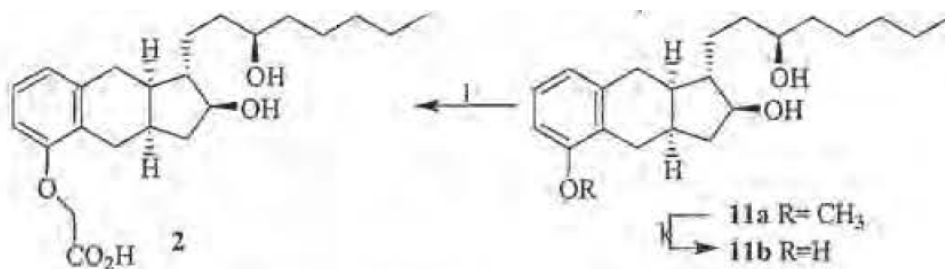


The figure above shows the structure of treprostinil diethanolamine salt. *Id.* at 96 (claim 49).

Phares teaches two crystalline forms of treprostinil diethanolamine salt, the metastable Form A and the thermodynamically more stable Form B.

Id. at 85. Phares states that “[a] particularly preferred embodiment of the present invention is form B of treprostinil diethanolamine.” *Id.* at 9.

Phares teaches the synthesis of (-)-treprostinil, the enantiomer of (+)-treprostinil. *Id.* at 39–40. Specifically, Phares teaches the following reaction procedure:



Id. at 40. The figure above shows the reaction procedure for the conversion of 11b to 2. *Id.* Phares describe it as: “(1) i. ClCH₂CN, K₂CO₃. ii, KOH, CH₃OH, reflux. 83% (2 steps).” *Id.*

Phares further teaches that “the enantiomer of the commercial drug (+)-treprostinil was synthesized using the stereoselective intramolecular Pauson Khand reaction as a key step and Mitsunobu inversion of the side-chain hydroxyl group.” *Id.*, *see also id.* at 39 (“Enantiomers of these compounds . . . can be synthesized using reagents and synthons of enantiomeric chirality of the above reagents.”).

C. Claim Construction

In an *inter partes* review, we construe a claim term “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b).” 37 C.F.R. § 42.100(b). Under that standard, the words of a claim “are generally given their ordinary and customary meaning,” which is “the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e.,

as of the effective filing date of the patent application.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

1. “Pharmaceutical Batch”

In the Petition, Petitioner argues that no construction of claim terms is required and “[a]ll terms should be given their plain and ordinary meaning in the art” at the priority date of the ’901 patent. Pet. 18–19. In the Preliminary Response, Patent Owner emphasizes the difference between a “compound,” as recited in the claims of the ’393 patent, and a “pharmaceutical batch,” as recited in challenged claim 1. Paper 6 (“Prelim. Resp.”), 8. In proposing the construction for “pharmaceutical batch,” Patent Owner relies on the FDA definition of “batch.” *Id.* at 9.

In our Decision to Institute, we generally agreed with Patent Owner’s proposed construction that

The POSA viewing the ’901 patent claims in light of the ’901 patent specification would have understood claim 1’s ‘pharmaceutical batch’ to be a specific quantity of treprostinil (or its salt) that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture, wherein the uniform character and quality is such that it still contains impurities resulting from the method by which it is produced.

Dec. 15–16 (quoting Prelim. Resp. 9). Later, in our Decision Denying Patent Owner’s Request on Rehearing of Decision on Institution, we clarified that “we did not construe the term ‘pharmaceutical batch’ in claim 1 to require storage stability.” Paper 14, 6 (citing Dec. 15–16).

In its Reply, Petitioner argues that Patent Owner’s construction of “pharmaceutical batch” “pulls language directly from FDA regulations” and

“creates more ambiguity than clarity by introducing terms that themselves would require construction.” Reply 4 (internal quotation marks omitted). According to Petitioner, “a POSA would understand ‘pharmaceutical batch’ to mean one ‘made according to the process recited in steps (a)–(d) and optionally (e), wherein no purification steps appear between alkylation and salt formation.’” *Id.* at 5. Petitioner further argues that “under either construction, Moriarty discloses a ‘pharmaceutical batch’ of 500g.” *Id.* at 6.

As discussed below, we agree with Petitioner that the challenged claims exclude any isolation⁶ between the alkylation and salt formation steps. *See infra*, Section II.C.3. That interpretation, however, flows from the language “contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil,” and not “pharmaceutical batch.” *Id.* As a result, we decline to adopt Petitioner’s proposed construction of “pharmaceutical batch.”

Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). Here, we do not need to define the outer bounds of the term “pharmaceutical batch” because the parties’ dispute over this term centers on the issue of storage stability.⁷ Patent Owner argues “the correct construction

⁶ The parties use the terms “purification” and “isolation” interchangeably in the papers. We use the term “isolation” in this Decision.

⁷ The parties agree on the “pharmaceutical” aspect of the term. We note the ’901 patent defines “pharmaceutically acceptable” as “being useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable and includes being useful for veterinary use as well as human pharmaceutical use.” Ex. 1001, 5:27–31.

of ‘pharmaceutical batch’ requires storage stability such that the batch could be stored stably for a period of time customary in pharmaceutical manufacturing.” PO Resp. 43 (citing Ex. 2025 ¶ 78)). Petitioner contends otherwise. Reply 6 (arguing Patent Owner’s construction “imports storage limitations into ‘pharmaceutical batch’ (POR9), but the Board’s construction did not (Dec. at 15-16)”). We agree with Petitioner.

Patent Owner supports its argument, relying on the testimony of Dr. Pinal, who in turn relies on the definitions of “batch,” “in-process material,” and “lot” in the FDA regulations. Ex. 2025 ¶ 78 (citing Ex. 2004, 133–34). Even if we consider the FDA regulations, none of the cited definitions mentions, let alone requires, storage. Thus, we reiterate that the term “pharmaceutical batch” in claim 1 does not require storage stability. *See* Paper 14, 6. This determination as to the scope of “pharmaceutical batch” is sufficient for purposes of this Decision, and we need not further address the term.

2. “Storing”/“Storage”

Claim 6 recites “storing a pharmaceutical batch of a salt of treprostinil as claimed in claim 1 at ambient temperature, and preparing a pharmaceutical product from the pharmaceutical batch after storage.” In our Decision to Institute, we agreed with Patent Owner that the terms “storing”/“storage” “require that the stored material possesses stability sufficient to allow manufacture and which maintains integrity for a sufficient period of time to be useful for the preparation of a pharmaceutical product.” Dec. 17 (quoting Prelim. Resp. 11).

In its Response, Patent Owner maintains its proposed claim construction. PO Resp. 11. Together with its Response, Patent Owner submitted the Prosecution History of Application No. 13/933,623 (“the ’623 application”) (Ex. 2028). The ’623 application, issued as Patent No. 9,156,786 (the ’786 patent), is the parent of the application that issued as the challenged ’901 patent. *See* Ex. 1001, code (63); Ex. 2028, 264.

Petitioner asserts that Patent Owner’s proposed construction is “inconsistent with its construction of this same term during prosecution of the ’901 Patent’s parent, the ’786 Patent.” Reply 7. We agree.

During the prosecution of the ’623 application, the applicant amended pending claim 1 as following:

1. (Currently Amended) A process for preparing a pharmaceutical product comprising treprostinil or a treprostinil salt, comprising:

combining treprostinil and a base in solution to form a base addition salt;

allowing crystallization of the base addition salt of treprostinil;
[[and]]

collecting the base addition salt of treprostinil, storing the collected base addition salt, and preparing a pharmaceutical product comprising treprostinil or a treprostinil salt from the base addition salt after storage.

Ex. 2028, 159. The examiner rejected this claim as obvious over Phares and another prior art reference. *Id.* at 172. The examiner specifically addressed the limitation directed to storing the treprostinil salt. *Id.* at 173–74.

According to the examiner,

The step of storing the treprostinil diethanolamine salt is inherently met by Phares. Examiner is interpreting the term

“storing” to mean a time period between preparation of treprostinil salt and its use in preparation of a pharmaceutical product. Said limitation is inherently met by Phares. Phares teaches preparation of pharmaceutical products and administration of said compounds to a subject (paragraphs [0049], [0071], [0072], [0074]). It is inherent that some time elapses between preparation of a compound and its use in preparation of a pharmaceutical formulation. Phares describes obtaining an X-ray diffraction spectrum of treprostinil diethanolamine. It is inherent that while obtaining the X-ray diffraction spectrum the compound is being stored.

Id.

In response, the applicant further amended the relevant part of the claim to “storing the collected base addition salt at ambient temperature, and preparing a pharmaceutical product comprising treprostinil or a treprostinil salt from the base addition salt after the storage.” *Id.* at 189. Relying on a Rule 132 Declaration of Dr. Liang Guo, the applicant argued:

[T]he PTO’s interpretation of the term “storing” is too broad even under the broadest reasonable interpretation standard. Even under the broadest reasonable interpretation standard, the PTO may not erase the meaning of a step in a method claim that is tied to the preamble. The claim is directed to “preparing a pharmaceutical product.” In the accompanying Guo Declaration, Dr. Liang Guo explains that a person of ordinary skill in the art would recognize that the term “stored” in the expression “crude treprostinil salts can be stored as raw material at ambient temperature” in paragraph 0046 of the specification as filed means stored for a period of at least three months. Guo Declaration at ¶ 6. Thus, “storing” in the context of “preparing a pharmaceutical product” would be understood by one of ordinary skill in the art to mean a period of at least three months. Based on this understanding of “storing,” Phares clearly does not meet the storing element of claim 1.

Id. at 193; *see also id.* at 198 (Guo Declaration ¶ 6 stating the same). The examiner, apparently finding this argument persuasive, allowed the claims thereafter. *Id.* at 243–44.

“[A]n invention is construed not only in the light of the claims, but also with reference to the file wrapper or prosecution history in the Patent Office.” *Graham*, 383 U.S. 1, 33. “The prosecution history of a related patent can be relevant if . . . it addresses a limitation in common with the patent in suit.” *Advanced Cardiovascular Sys., Inc. v. Medtronic, Inc.*, 265 F.3d 1294, 1305 (Fed. Cir. 2001); *see also Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 980 (Fed. Cir. 1999) (“When multiple patents derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents that contain the same claim limitation.”).

Here, the Specification of the ’901 patent includes the same language “crude treprostinil salts can be stored as raw material at ambient temperature” addressed in the prosecution of the parent ’623 application. Ex. 1001, 17:5–6. More importantly, challenged claim 6 recites the same limitation “preparing a pharmaceutical product . . . after storage” the applicant expressly interpreted there. *See* Ex. 2028, 193. Because “the same claim limitation is at issue, prosecution disclaimer made on the same limitation in an ancestor application will attach,” the applicant’s interpretation of “storing”/“storage” during the prosecution of the ’623 application applies here. *See Omega Eng’g, Inc., v. Raytek Corp.*, 334 F.3d 1314, 1333 (Fed. Cir. 2003).

In the parallel district court case, the court accorded the terms “stored”/“storing”/“storage” their plain and ordinary meaning. Ex. 2035,⁸ 1. Under 37 C.F.R. § 42.100(b), we have considered the district court’s claim construction. In this case, however, the prosecution history, part of the intrinsic evidence, is so unambiguous that we must apply the applicant’s interpretation presented therein. *See Chimie v. PPG Indus., Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005) (“The purpose of consulting the prosecution history in construing a claim is to exclude any interpretation that was disclaimed during prosecution.”); *Phillips*, 415 F.3d at 1317.

Petitioner points out that Patent Owner’s expert in the parallel district court case, Dr. Robert R. Ruffolo, opined that, in the ’901 patent, actual storage was not required.⁹ Paper 29, 3–5 (citing Ex. 2034, 130:12–132:4, 132:15–136:11). We acknowledge Dr. Ruffolo’s testimony that claim 6 does not require that the pharmaceutical product be made after storage of the pharmaceutical batch of a salt of treprostinil. *See* Ex. 2034, 136:7–11. Claim 6, however, explicitly recites storing a pharmaceutical batch of a salt of treprostinil, and preparing a pharmaceutical product from the pharmaceutical batch after storage. Thus, we discount the cited Ruffolo testimony on “storage” because it “is clearly at odds with the claim construction mandated by the claims themselves.” *See Phillips*, 415 F.3d

⁸ The parties agreed to submit the claim construction order from the district court case (Ex. 2035) as supplemental information. Paper 40, 2.

⁹ Petitioner asks us to strike “Patent Owner’s Submissions Regarding ‘Storage’” in Patent Owner Response, Sur-reply, and the two declarations of Dr. Pinal (Exs. 2002, 2025). Paper 29, 8. We address this issue below in Section IV.

at 1318; *see also id.* at 1324 (holding extrinsic evidence cannot be used to “contradict claim meaning that is unambiguous in light of the intrinsic evidence”).

In sum, we determine that claim 6 requires actual storage, and in view of the applicant’s statements during the prosecution of the parent ’623 application, we determine the terms “storing”/“storage” in the context of “preparing a pharmaceutical product” require storing or storage for a period of at least three months.

3. Step (c) of Challenged Claim 1

Step (c) of challenged claim 1 recites “contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil.” In its Response, Patent Owner points out that “[t]he claim’s preamble requires the pharmaceutical batch be one ‘consisting of’ what results from the recited steps.” PO Resp. 11. According to Patent Owner, “[t]ogether, this language means treprostinil is not isolated from the solution formed in step (b) before forming a salt in step (c).” *Id.* Petitioner does not contest Patent Owner’s proposed construction. Reply 3 n.2.

Later, however, Patent Owner retracts its argument, apparently in response to certain disputes between the parties in the co-pending district court case. Sur-reply 8. Relying on the testimony of Dr. Pinal, Patent Owner points out claim 5 of the ’066 patent recites “the base is combined with treprostinil that has not been previously isolated.” Ex. 2025 ¶ 157 (quoting Ex. 2027, 18:31–33); Sur-reply 8 (citing Ex. 2025 ¶ 157). In contrast, Patent Owner argues “not isolating the treprostinil before contacting it with a base

is **not** an explicit limitation of claim 1 of the '901 patent.” Sur-reply 8 (quoting Ex. 2025 ¶ 157 (emphasis added by Patent Owner)).

Patent Owner also relies on the testimony of Dr. Ruffolo in the parallel district court case. *Id.* at 8–9 (citing Ex. 2033 ¶ 15; Ex. 2034, 247–48). According to Dr. Ruffolo, “a POSA would understand that the passage in the Patent Owner’s Response upon which [Petitioner] Liquidia relies is incorrect to the degree it suggests that Examples 2 and 3 describe synthesizing treprostinil without isolating it prior to salt formation.”

Ex. 2033 ¶ 15. Patent Owner argues:

[PO Resp.] at 11 inaccurately suggests that the language of claim 1 means treprostinil is “not isolated” from the solution formed in step (b) before forming a salt in step (c). *See, e.g.*, POR, 15, 29, 34, 53 . . . These statements are unsupported and a POSA would not have understood them as consistent with the claims read in light of the specification.

Sur-reply 8. As a result, Patent Owner states that it “withdraws those statements.”¹⁰ *Id.* at 9; *see also* Paper 29, 1.

Whether Patent Owner is allowed to withdraw its arguments regarding step (c) does not have any effect on our construction of step (c). This is because “[w]hen construing claim terms, we first look to, and primarily rely on, the intrinsic evidence, including the claims themselves, the specification, and the prosecution history of the patent, which is usually dispositive.”

¹⁰ Petitioner argues that if Patent Owner is permitted to withdraw the statements related to the issue of “not isolated,” then we should strike not only those in Patent Owner Response, as identified by Patent Owner, but also many other statements in the Patent Owner Response, the Pinal Declarations (Exs. 2002, 2025), and the Sur-reply. Paper 29, 1–2. We address this issue below in Section IV.

Sunovion Pharm., Inc. v. Teva Pharm. USA, Inc., 731 F.3d 1271, 1276 (Fed. Cir. 2013). Here, step (c) of challenged claim 1 requires “contacting the solution comprising treprostinil *from step (b)* with a base to form a salt of treprostinil.” Ex. 1001, 17:27–29 (emphasis added). The claim language itself, thus, dictates that the solution formed in step (b), and not treprostinil isolated from step (b), is the starting material for forming a salt in step (c).

The Specification of the ’901 patent supports our determination. Indeed, the Specification touts that one of the advantages of the disclosed process is that “the treprostinil salts can be synthesized from the solution of treprostinil without isolation,” because “[t]he impurities carried over from intermediate steps (i.e. alkylation of triol and hydrolysis of benzindene nitrile) are removed during the carbon treatment and the salt formation step.” Ex. 1001, 17:1–11. As a result, we agree with the argument presented in the Patent Owner Response that “claim 1 requires the solution in which treprostinil is formed be used directly in the next salt-forming step without isolating treprostinil in between.” *See* PO Resp. 11.

The testimony of Dr. Pinal and Dr. Ruffolo do not change our determination. First, extrinsic evidence in the form of expert testimony, although useful at times, cannot be used to “contradict claim meaning that is unambiguous in light of the intrinsic evidence.” *Phillips*, 415 F.3d at 1324. Because the testimony of Patent Owner’s experts on this issue are “clearly at odds with the claim construction mandated by the claims themselves,” we accord them little weight. *See id.* at 1318.

Second, “extrinsic evidence consisting of expert reports and testimony is generated at the time of and for the purpose of litigation and thus can

suffer from bias that is not present in intrinsic evidence.” *Id.* at 1318. Here, Dr. Ruffolo indicated that his testimony was prepared specifically in response to Petitioner’s “documentary evidence that treprostinil in [Petitioner] Liquidia’s LIQ861 is isolated prior to salt formation and cannot infringe.” Ex. 2033 ¶ 4. Thus, the testimony of Dr. Ruffolo on this issue are not sufficiently reliable.

Third, Patent Owner’s reliance on claim 5 of the ’066 patent is unavailing. Patent Owner argues when it “wants to exclude purification from its claim . . . it knows specifically how to do that.” Tr. 56:20–22. Patent Owner essentially invites us to assume that, as an applicant, it always follows the same pattern of claiming. We decline to do so and do not construe step (c) of challenged claim 1 based on the entirely different language in claim 5 of the ’066 patent.

In sum, in view of the intrinsic evidence, including the claim language and the Specification, we conclude that treprostinil is not isolated from the solution formed in step (b) before forming a salt in step (c).

D. Level of Ordinary Skill

In the Decision to Institute, we found “the level of ordinary skill in the art is reflected by the prior art, including Phares and Moriarty.” Dec. 22. Patent Owner argues that the challenged claims “contemplate batch-scale synthesis and late-stage chemical purification.” PO Resp. 23. According to Patent Owner, “scaling up is a separate and difficult process.” *Id.* at 24. Thus, Patent Owner contends that an ordinarily skilled artisan “would have been an industrial chemist or chemical engineer with experience in

pharmaceutical manufacturing.” *Id.* at 23. We find Patent Owner’s definition of the skill level too narrow.

Patent Owner relies on the declaration of Dr. Pinal, who testifies that the ’901 patent is “focused on the production of pharmaceutical compositions and products, on a commercial batch-size scale.” Ex. 2002 ¶ 91; *see also id.* ¶ 92 (opining that organic and medicinal chemists do not have the “requisite skill set for the large-scale manufacture” of drugs); PO Resp. 24 (arguing an ordinarily skilled artisan is aware of “problems encountered in preparing a commercial-scale pharmaceutical product”).

Patent Owner does not explain what “a commercial batch-size scale,” a “large-scale,” or “a commercial-scale” encompasses. Moreover, during his deposition, Dr. Pinal, Patent Owner’s expert, testified that a pharmaceutical product is not limited to a commercial one, and many of them are in clinical trials. Ex. 1018, 111:17–112:8. And during the oral argument, counsel for Patent Owner acknowledged that a compounding pharmacy can also make a pharmaceutical batch. Tr. 47:11–20.

Patent Owner emphasizes the “distinction between the academic and the practical.” PO Resp. 24 (citing Ex. 2025 ¶¶ 55–63). Dr. Pinal testifies that “[o]ne cannot overemphasize that benchtop synthetic chemistry is not a viable replacement for, i.e., closely related to, the commercial production of pharmaceutical drug products, which is performed to high scale, in a pilot plant, kilo-lab plant, or manufacturing plant.” Ex. 2025 ¶ 55.

Challenged claim 1 requires “the pharmaceutical batch contains at least 2.9 g of treprostinil or its salt.” In comparison, Moriarty teaches the synthesis of 441 grams of treprostinil. Ex. 1009, 13. Indeed, treprostinil had

been prepared as described in Moriarty, and used as the active ingredient in Remodulin. Ex. 1001, 1:27–32. And the '901 patent itself describes the Moriarty process as having “[b]atch size: 500 g” with a yield of treprostinil of “~535 g.” *Id.* at 15:38, 16:7, 16:60. Yet, Dr. Pinal characterizes Moriarty as on a “benchtop” scale. Ex. 2025 ¶ 92. This inconsistency casts further doubt over Dr. Pinal’s testimony on this issue.

We also note that Phares teaches not one, but two, clinical studies with treprostinil diethanolamine. Ex. 1008, 82–86. As Dr. Pinal acknowledged during his deposition, pharmaceutical products include those used in clinical trials, even if they are used only in clinical trials. Ex. 1018, 111:17–112:8. Thus, Phares reflects the skill level, even under Patent Owner’s construction.

Patent Owner challenges Dr. Winkler’s qualification to provide expert testimony. *See, e.g.*, PO Resp. 23 n.2 (“Prof. Winkler frames the issues in terms of academic and undergraduate lab organic chemistry because that is where his experience lies.”); Paper 31,¹¹ 4 (“Dr. Winkler is unqualified to testify on the relevant subject matter.”). We are not persuaded.

¹¹ Patent Owner argues that Dr. Winkler does not have qualifications in the relevant field even under Petitioner’s own definition of the skill level, as stated in the Declaration of Dr. Hall-Ellis. Paper 31, 4 (citing Ex. 1015 ¶ 16). Dr. Hall-Ellis, in her Declaration in support of the Petition, testified that an ordinarily skilled artisan is “a medical physicist” with “experience in radiation oncology physics.” Ex. 1015 ¶ 16. Petitioner later filed a supplemental Hall-Ellis Declaration to correct that error. *See* Ex. 1052.

“A person may not need to be a person of ordinary skill in the art in order to testify as an expert under Rule 702, but rather must be qualified in the pertinent art.” Patent Trial and Appeal Board Consolidated Trial Practice Guide¹² 34 (“There is . . . no requirement of a perfect match between the expert’s experience and the relevant field.”). Here, we are satisfied that Dr. Winkler qualifies as an expert witness “by knowledge, skill, experience, training, or education to testify in the form of an opinion.” *See id.*; Ex. 1003.

In sum, after considering the full record developed at trial, we maintain that the level of ordinary skill in the art is reflected by the prior art, including Phares and Moriarty. We further note that our analyses and legal conclusions apply with equal force under the skill level as defined by either party.

E. Obviousness over Phares and Moriarty

Petitioner argues that claims 1–9 of the ’901 patent would have been obvious over Moriarty and Phares. Pet. 49–75. After reviewing the entire record, we conclude Petitioner has shown by a preponderance of the evidence that the combination of Moriarty and Phares renders claims 1–5, 8, and 9 obvious. Petitioner, however, has not shown by a preponderance of the evidence that the combination of Moriarty and Phares renders claims 6 and 7 obvious.

¹² Available at <https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf>.

1. Claims 1–5, 8, and 9

i. Claim 1

Regarding claim 1, Petitioner points out that Moriarty describes synthesizing treprostinil via the stereoselective intramolecular Pauson-Khand cyclization, and Phares teaches forming treprostinil diethanolamine salt having the same structure as disclosed in the '901 patent. Pet. 53–55 (citing Ex. 1008, 9, 22, 96; Ex. 1009, 1). According to Petitioner, “[t]he combination of Moriarty and Phares discloses the same process steps and product of the '901 patent and as such, the combination of these references would disclose a purity of at least equal purity to that claimed in the '901 patent.” *Id.* at 56 (citing Ex. 1002 ¶ 159). In addition, Phares teaches “the pharmaceutical acceptability of the compounds.” *Id.* at 29 (citing Ex. 1008, 22). Thus, Petitioner concludes “Moriarty in combination with Phares disclose a pharmaceutical batch consisting of treprostinil or a salt thereof and impurities,” as recited in challenged claim 1. *Id.* at 56.

Specifically, Petitioner refers to Moriarty for teaching alkylating benzindene triol 34 to yield nitrile 35, and hydrolyzing nitrile 35 to yield treprostinil. *Id.* at 57, 59 (citing Ex. 1009, 6, 8, 13). Thus, Petitioner contends that Moriarty teaches steps (a) and (b) of challenged claim 1.

Acknowledging that step (c), “the step of reacting treprostinil with a base to form a salt of 7 is not disclosed in Moriarty,” Petitioner asserts “this step is clearly disclosed in Phares.” *Id.* at 54. Petitioner refers to Phares for teaching dissolving treprostinil in a 1:1 molar ratio mixture of ethanol:water and then adding diethanolamine. *Id.* at 54, 61 (citing Ex. 1008, 22). Petitioner asserts that “a POSA would likely understand the treprostinil acid

disclosed at page 22 [of Phares] to have been isolated before addition of the base.” *Id.* at 61 (citing Ex. 1002 ¶ 176). But, according to Petitioner, “not isolating the treprostinil before contacting it with a base is obvious based on what is taught by Phares,” and “[a] POSA would be motivated to do so to save a step of isolation.” *Id.* (citing Ex. 1002 ¶¶ 177, 178; Ex. 1008; 40).

Petitioner argues that Phares also teaches step (d) because it is needed to form the disclosed crystalline forms of treprostinil diethanolamine salt.¹³ *Id.* at 62 (citing Ex. 1008, 85–89).

Regarding the wherein clause reciting “the pharmaceutical batch contains at least 2.9 g of treprostinil or its salt,” Moriarty teaches that “[t]he essential requirements for any large-scale, multistep synthesis of a molecule of the complexity of [treprostinil] are very high overall stereoselectivity, high overall chemical yield, and scalability of individual steps to multigram quantities.” Ex. 1009, 3. Petitioner refers to Moriarty for synthesizing 441 g of treprostinil. Pet. 63 (citing Ex. 1009, 13).

Petitioner contends that an ordinarily skilled artisan would have had a reason to combine Moriarty and Phares because “Phares is directed to improving treprostinil, and the Moriarty process . . . was a well-known way to make treprostinil.” *Id.* at 51–52 (citing Ex. 1002 ¶¶ 148, 151). Petitioner further asserts that an ordinarily skilled artisan would have had a reasonable expectation of success in combining the references because “[t]he proposed combination of Moriarty and Phares yields treprostinil diethanolamine

¹³ We do not discuss step (e) because it is an optional step.

salt . . . via the process taught by Phares,” and “Phares successfully performed precisely that step.” *Id.* at 52–53 (citing Ex. 1002 ¶ 152).

After reviewing the entire record developed at trial, and as explained below, we determine Petitioner has shown, by a preponderance of the evidence, that the combination of Moriarty and Phares teaches each limitation of challenged claim 1. Petitioner has also shown that an ordinarily skilled artisan would have had a reason to combine Moriarty and Phares, and would have had a reasonable expectation of success when doing so.

Patent Owner does not dispute that the combination of Moriarty and Phares teaches steps (a), (b), and (d) of challenged claim 1.¹⁴ Patent Owner also does not dispute that the combined teachings suggest the “at least 2.9 g of treprostinil or its salt” as recited in the wherein clause. Patent Owner, however, challenges Petitioner’s accounting of step (c) of claim 1, asserting that “claim 1’s recited steps differ from Phares and Moriarty because they do not involve isolation of treprostinil intermediate.”¹⁵ PO Resp. 57; *see also id.*

¹⁴ Patent Owner argues that Phares contains “an insufficient disclosure to provide the POSA with enough conditions to successfully recrystallize [tritreprostinil diethanolamine].” *Id.* at 55. To the extent Patent Owner challenges Phares for not being enabling, this argument is unavailing. “Under § 103 . . . a reference need not be enabled; it qualifies as a prior art, regardless, for whatever is disclosed therein.” *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1357 (Fed. Cir. 2003) (instructing the trial court to reconsider obviousness on remand “without reference to whether [the prior art] is enabled, as enablement of the prior art is not a requirement to prove invalidity under § 103”).

¹⁵ Petitioner asks us to strike this and other arguments because Patent Owner seeks to withdraw some statements related to the “no isolation” argument.

at 62 (“[T]he recited steps are different from those disclosed in Moriarty and Phares (no isolation of treprostinil after alkylation and hydrolysis steps before forming a salt).”). Patent Owner also asserts that the product from the combination of Moriarty and Phares does not necessarily include the same impurities as recited in claim 1. *Id.* at 62–64. In addition, Patent Owner contends that Phares and Moriarty are directed to different problems. *Id.* at 54–56. According to Patent Owner, Petitioner “has failed to demonstrate that a POSA would have had the requisite motivation and expectation of success.” *Id.* at 58. We address these contentions below.

a. Reason to Combine and Modify

Moriarty teaches synthesis of treprostinil “via the stereoselective intramolecular Pauson-Khand cyclization.” Ex. 1009, 1. Similarly, Phares teaches that “the enantiomer of the commercial drug (+)-Treprostinil was synthesized using the stereoselective intramolecular Pauson Khand reaction as a key step.” Ex. 1008, 40. Thus, we find that the two references are not directed to problems so different that an ordinarily skilled artisan would not have combined their teachings.

Paper 29, 1–2. We address those requests below in Section IV. Our obviousness analysis, however, remains the same regardless of whether we grant Petitioner’s request to strike. This is because, as explained above, based on the intrinsic evidence, we construe claim 1 to exclude isolation between steps (b) and (c). *See supra*, Section II.C.3. Thus, Petitioner must show, with or without Patent Owner’s arguments, that the combined teachings of Moriarty and Phares suggest to an ordinarily skilled artisan to skip the intermediate isolation step.

Petitioner asserts that one reason to combine Moriarty and Phares is because “Phares is directed to improving treprostinil, and the Moriarty process . . . was a well-known way to make treprostinil.” Pet. 51–52. This assertion is supported not only by the Winkler Declaration (Ex. 1002 ¶ 151), but also by the testimony of Dr. Pinal, Patent Owner’s expert. Indeed, Dr. Pinal recognized, “[t]he end of Moriarty is the beginning of Phares.” Ex. 1018, 135:6; *see also id.* at 135:16–19 (“Moriarty teaches how to make treprostinil and Phares teaches how to take that treprostinil and further modify it to produce other molecular entities.”). As Patent Owner acknowledges, “Phares identifies the diethanolamine salt as a preferred embodiment.” PO Resp. 61; Ex. 1008, 9. Thus, we are persuaded that an ordinarily skilled artisan would have had a reason to start with the treprostinil free acid of Moriarty and convert it into the diethanolamine salt.

Phares teaches “treprostinil as the free acid has an absolute oral bioavailability of less than 10%.” Ex.1008, 2. According to Patent Owner, this shows “[i]f anything, Phares teaches away from the preparation of treprostinil for use as a pharmaceutical product.” PO Resp. 55. We disagree.

As Petitioner argues, an ordinarily skilled artisan would have had a reason to combine Moriarty and Phares because “Phares is directed to improving treprostinil.” Pet. 51. One of the improvements is on the bioavailability. *See* Reply 13 (citing Ex. 1017 ¶ 128); Ex. 1008, 83 (“Based on historical intravenous treprostinil sodium data, the mean absolute bioavailability values for the 0.2 mg, 0.5 mg, 1.0 mg and 2.0 mg doses of UT-15C [treprostinil diethanolamine] were estimated to be 21%, 23%, 24% and 25%, respectively.”).

Patent Owner contends that, if Petitioner were right that “the claimed invention may have *worse* purity than Moriarty and Phares,” then “a POSA would have no motivation to change Moriarty at all.” PO Resp. 56 (citing Pet. 56; Ex. 2025 ¶ 250). Patent Owner’s contention is unavailing.

“[T]he problem motivating the patentee may be only one of many addressed by the patent’s subject matter.” *KSR*, 550 U.S. at 420; *see In re Kahn*, 441 F.3d 977, 990 (Fed. Cir. 2006) (stating that an ordinarily skilled artisan need not be motivated to combine prior art for the same reason contemplated by the inventor). Here, by taking treprostinil of Moriarty and “further modify[ing] it to produce other molecular entities” (Ex. 1018, 135:16–19), such as treprostinil diethanolamine, Phares, even if it does not improve the purity, improves at least the bioavailability, of treprostinil of Moriarty. *See* Ex. 1008, 2, 83. This provides a sufficient reason for an ordinarily skilled artisan to combine the teachings of Moriarty and Phares.

b. Step (c) and Recited Impurities

Dr. Winkler testifies that, in Phares, “[t]reatment of Compound **11b** with KOH, CH₃OH (methanol) . . . would lead to the formation of a solution of treprostinil carboxylic acid after neutralization.” Ex. 1002 ¶ 174. “[I]nstead of isolating the neutral carboxylic acid at this step by removal of the methanol,” Dr. Winkler continues, “one could instead add diethanolamine (i.e., a base) to the treprostinil solution so that removal of the methanol would instead leave a salt, specifically, treprostinil diethanolamine salt.” *Id.* ¶ 177. According to Dr. Winkler, “[a] POSA would understand that an intermediate purification step is unnecessary because not purifying the intermediate carboxylic acid before addition of a base does not affect salt

formation.” *Id.* ¶ 151. Relying on the testimony of Dr. Winkler, Petitioner argues that “a POSA would have sought to combine Moriarty and Phares in order to eliminate the intermediate purification step taught by Moriarty, thereby increasing synthetic efficiency and lowering production costs for treprostinil diethanolamine salt.” Pet. 52 (citing Ex. 1002 ¶ 151).

Patent Owner argues that Petitioner “cannot identify support in the asserted art or the background references for these motivations.” PO Resp. 61–62. Instead, according to Patent Owner, Petitioner’s “proffered motivations—increasing synthetic efficiency and lowering production costs—simply restate two advantages identified in the ’901 patent: reducing solvents and labor.” *Id.* at 61.

Patent Owner’s arguments are unavailing because “there is no requirement that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art.” *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1361 (Fed. Cir. 2006). Thus, Petitioner is not required to cite to prior art for expressly disclosing the elimination of the intermediate isolation step.

This is especially true here because “the desire to enhance commercial opportunities by improving a product or process is universal—and even common-sensical.” *Id.* at 1368. After all, there is an implicit motivation to combine or to modify prior art teachings when the improvement is technology-independent and the combination or modification “results in a product or process that is more desirable, for example because it is stronger,

cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient.” *Id.* Such is the case here. We are persuaded that an ordinarily skilled artisan would have had a reason to eliminate the intermediate isolation step, “thereby increasing synthetic efficiency and lowering production costs for treprostinil diethanolamine salt.” Pet. 52; Reply 15; Ex. 1017 ¶¶ 140–144. Thus, we are persuaded that the combination of Moriarty and Phares teaches step (c) of challenged claim 1.

Having decided that an ordinarily skilled artisan would have combined the teachings of Moriarty and Phares, and the combination teaches each required step of challenged claim 1, we turn to Patent Owner’s argument that “[a] product from Moriarty and Phares does not inherently include the same resulting impurities.” PO Resp. 62. We reject this argument because it is based on an incorrect premise.

Patent Owner contends that “[i]nherency requires identity of steps before inherency can be inferred.” *Id.* According to Patent Owner, “the recited steps [of claim 1] are different from those disclosed in Moriarty and Phares.” *Id.* In its Response, Patent Owner alleges that in claim 1, there is “no isolation of treprostinil after alkylation and hydrolysis steps before forming a salt.” *Id.* Patent Owner later seeks to withdraw this statement (Paper 29, 1) but does not explain what other differences exist between the combined prior art teachings and the required steps of claim 1.

As explained above, we are persuaded by Petitioner’s evidence and arguments that the combination of Moriarty and Phares teaches the same process steps as those required in challenged claim 1. Thus, we agree with Petitioner that the product from those steps would include the same resulting

impurities. *See* Pet. 56; Reply 17 (pointing out that claim 1 recites only “impurities *resulting from*” the steps, without identifying any specific “type” of impurity, and without specifying the solvents and reagent required to perform the steps).

c. Reasonable Expectation of Success

Patent Owner also asserts that Petitioner has not shown an ordinarily skilled artisan would eliminate the intermediate isolation step with a reasonable expectation of success.¹⁶ PO Resp. 30–34. Patent Owner argues Petitioner “ignores the practical realities.” *Id.* at 30. According to Patent Owner, “a POSA would not know if the proposed step elimination would work,” because “in the context of large-scale pharmaceutical manufacturing involving batch production, elimination of an intermediate isolation step has unpredictable impacts on the purity and quality of a final product.” *Id.* at 32 (citing Ex. 2025 ¶¶ 158, 289–297), 34 (quotation marks omitted). Patent Owner’s arguments are unavailing.

¹⁶ Under the ground based on Moriarty and Phares, Patent Owner argues that Petitioner “failed to demonstrate a motivation to combine the references to meet the recited claim limitations with a reasonable expectation of success.” PO Resp. 52; *see also id.* at 58 (the same). Patent Owner, however, does not provide sufficient analysis to undermine Petitioner’s showing of reasonable expectation of success. *See Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (explaining the motivation and reasonable expectation inquiries are different inquiries, and the latter refers to likelihood of success in modifying the prior art to reach the claimed invention). For the sake of completeness, we address here Patent Owner’s arguments related to reasonable expectation of success that Patent Owner proffered under the ground based on Phares alone.

Relying on Dr. Winkler's testimony, Petitioner argues "[t]he formation of a carboxylate salt, by the addition of a base to a neutral carboxylic acid, and the subsequent addition of a strong acid to regenerate carboxylic acid, as disclosed in claims 1 and 8 are standard chemistry purification procedures." Pet. 22–23 (citing Ex. 1002 ¶ 47); *see also* Ex. 1002 ¶ 48 (citing Exs. 1010, 1011). "More specifically," according to Petitioner, "contacting a carboxylic acid of a prostacyclin derivative, such as treprostinil, with a base to form a salt, followed by the addition of a strong acid to regenerate the carboxylic acid, was a well-known chemical purification technique in the prior art." Pet. 23–24 (citing Ex. 1002 ¶ 49); *see also* Ex. 1002 ¶ 49 (citing Exs. 1012, 1013).

One of the prior art references Dr. Winkler relies on is Kawakami.¹⁷ *See* Ex. 1002 ¶ 49 (citing Kawakami to support the testimony that "contacting a carboxylic acid of a prostacyclin derivative, such as treprostinil, with a base to form a salt, followed by the addition of a strong acid to regenerate the carboxylic acid, was a well-known chemical purification technique in the prior art"), ¶ 157 (the same); *see also* Pet. 23–24 (citing Ex. 1002 ¶ 49), 55 (citing Ex. 1002 ¶ 157). Kawakami describes using dicyclohexylamine to form a crystalline dicyclohexylamine salt of a methanoprostacyclin derivative, in order to purify the methanoprostacyclin. Ex. 1012, 3. It teaches obtaining a dicyclohexylamine salt by "mixing a methanoprostacyclin derivative [I] . . . with dicyclohexylamine in an appropriate solvent." *Id.* at 5–6. According to

¹⁷ Translation of JP 56-122328, published Sept. 25, 1981 (Ex. 1012).

Kawakami, “[t]he dicyclohexylamine salt of the methanoprostacyclin derivative [I] thus obtained generally has fairly high purity, and the purity can be further improved by recrystallization as needed with the use of an appropriate solvent.” *Id.* at 6. Kawakami states “[t]he dicyclohexylamine salt obtained by the present invention can be easily reverted to a free methanoprostacyclin derivative [I] by conventional methods, and the resulting methanoprostacyclin derivative exhibits excellent crystallinity compared with substances not purified according to the present invention.” *Id.*

Dr. Winkler testifies that dicyclohexylamine is an amine base with similar reactivity to diethanolamine. Ex. 1002 ¶ 49; Ex. 1017 ¶ 108. Dr. Pinal, Patent Owner’s expert, disagrees. Ex. 2025 ¶¶ 180–184. According to Dr. Pinal, even though both dicyclohexylamine and diethanolamine are used as bases to form salts with acidic prostacyclins, they have different miscibilities, which means the salt formation processes using the two bases are “fundamentally different.” *Id.*

On this point, we agree with Dr. Winkler that “Dr. Pinal’s discussion of the relative miscibilities of dicyclohexylamine and diethanolamine is irrelevant, because both compounds are highly soluble in ethanol and the salt formation in Phares is taught in a 1:1 mixture of water and ethanol.” Ex. 1017 ¶ 109. We also agree with Dr. Winkler that “Kawakami teaches the purification of a methanoprostacyclin derivative by salt formation with a secondary amine, which is the same reaction as taught in Phares for the formation of the diethanolamine salt of treprostinil.” *Id.*

We also reject Patent Owner’s emphasis on “the context of large-scale pharmaceutical manufacturing involving batch production.” *See* PO Resp. 32. As explained above, it is unclear what this context means, especially given that Dr. Pinal characterizes 441 grams of treprostinil in Moriarty as on a “benchtop” scale, even though challenged claim 1 recites “2.9 g of treprostinil or its salt.” *See supra*, Section II.D.

Regardless, Kawakami recognizes that “establishment of an efficient and *industrially viable method* of separating isomers of methanoprostacyclin derivatives is essential in the development of these derivatives as *pharmaceutical products*.” Ex. 1012, 4 (emphases added). It is “[i]n view of” this goal that the Kawakami inventors “succeeded in inventing an extremely simple and *industrially viable purification method*.” *Id.* (emphasis added).

Thus, even taking the context of pharmaceutical manufacturing into consideration, we are persuaded that Kawakami “demonstrates that contacting a carboxylic acid of a prostacyclin derivative . . . with a base to form a salt, followed by the addition of a strong acid to regenerate the carboxylic acid, was a well-known chemical purification technique in the prior art.” Ex. 1017 ¶ 108. As a result, Petitioner has shown an ordinarily skilled artisan would have had a reasonable expectation of success in eliminating the intermediate isolation step.

d. Conclusion

After reviewing the record, we determine that Petitioner demonstrates by a preponderance of the evidence that the combination of Moriarty and Phares teaches each and every limitation of claim 1, and that an ordinarily

skilled artisan would have had a reason to implement these teachings to arrive at the subject matter of claim 1 with a reasonable expectation of success.

ii. Claims 2–5, 8, and 9

Petitioner provides analysis and citations to record evidence to show Moriarty and Phares teaches or suggests every additional limitation of claims 2–5, 8, and 9. Pet. 64–67, 70–75. Patent Owner does not argue these claims separately. Upon review of Petitioner’s arguments and the evidence of record, we adopt Petitioner’s mapping of the additional limitations of claims 2–5, 8, and 9 as our own findings.

In sum, we determine that Petitioner has demonstrated by a preponderance of the evidence that the combination of Moriarty and Phares teaches or suggests every additional limitation of claims 2–5, 8, and 9.

iii. Objective Indicia of Non-obviousness

Patent Owner contends that objective indicia demonstrates non-obviousness of the challenged claims. PO Resp. 66–69. We disagree.

Objective indicia of non-obviousness guard against hindsight reasoning in an obviousness analysis, and are often “the most probative and cogent evidence in the record.” *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1328 (Fed. Cir. 2016). As such, objective indicia of non-obviousness must be considered in every case in which they are presented. *Id.* Objective indicia of non-obviousness include commercial success, long-felt but unsolved needs, failure of others, copying, praise in the art, unexpected results, and industry acceptance. *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1129 (Fed. Cir. 2000).

Patent Owner begins by contending that the '901 patent “contains more than mere argument or conclusory statements; it contains specific data indicating improved properties.” PO Resp. 66 (quoting *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995)). Patent Owner follows that assertion by stating that the Specification “identifies a specific need,” when it explains that “Treprostinil, and other prostacyclin derivatives are of great importance from a medicinal point of view,” and therefore “a need exists for an efficient process to synthesize these compounds on a large scale suitable for commercial production.” *Id.* at 67 (quoting Ex. 1001, 1:66–2:3). According to Patent Owner, “[t]his disclosure emphasizes not only the greater benefit for large-scale synthesis but also the higher purity.” *Id.* (citing Ex. 1001, 6:4–18). Patent Owner asserts also that the Specification “illustrates these advantages with comparative data,” and refers us to other portions of the '901 patent to support that assertion. *Id.* In particular, Patent Owner contends the “storage stability as to the ‘pharmaceutical batch’ of claim 1 and its dependent claims” is an “unexpected advantage.” *Id.* at 68.

We begin by noting, as Petitioner has, that “unexpected advantage” is not a recognized secondary consideration. *See* Pet. Reply 26. Insofar as Patent Owner’s argument is considered be one addressing unexpected results, we find Patent’s Owner’s showing insufficient. As our reviewing court has instructed, to properly evaluate whether a superior property was unexpected, we must first consider what properties were expected. *See Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1371 (Fed. Cir. 2007). To do so, we consider the results of the closest prior art and compare them to those asserted for the claimed invention. *See In re Baxter Travenol Labs.*, 952

F.2d 388, 392 (Fed. Cir. 1991) (“[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.”). A showing of unexpected results must be commensurate in scope with the breadth of the claims. *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983).

As presented, Patent Owner’s arguments are conclusory at best and do not clearly identify what it considers to be the closest prior art or demonstrate how any alleged unexpected results were unexpected compared with the closest prior art. At most, Patent Owner provides a string citation to portions of the Specification and declaration testimony, without providing a discussion of the alleged evidence and explaining how it supports nonobviousness. Nor does Patent Owner demonstrate adequately that the alleged storage stability advantages were commensurate in scope with the breadth of the challenged. And as explained above, the term “pharmaceutical batch” in claim 1 does not require storage stability. *See supra*, Section II.C.1.

In view of the foregoing, we determine that Patent Owner’s evidence of objective indicia does not sufficiently demonstrate non-obviousness of claims 1–5, 8, and 9.

iv. Conclusion

Upon review of the record as a whole, including Patent Owner’s evidence of objective indicia, and for the reasons discussed above, we determine that Petitioner demonstrates by a preponderance of the evidence that the subject matter of claims 1–5, 8, and 9 would have been obvious over the combination of Moriarty and Phares.

2. Claims 6 and 7

Claim 6 is directed to “[a] method of preparing a pharmaceutical product from a pharmaceutical batch as claimed in claim 1, comprising storing a pharmaceutical batch of a salt of treprostinil as claimed in claim 1 at ambient temperature, and preparing a pharmaceutical product from the pharmaceutical batch after storage.” Claim 7 depends from claim 6, and specifies that “the salt of treprostinil is a diethanolamine salt.”

Petitioner argues that Phares inherently teaches the limitation of “storing”/“storage.” Pet. 68. Petitioner points out that Phares teaches two crystalline forms of treprostinil diethanolamine salt, Form A and Form B. *Id.* (citing Ex. 1008, 85–89). According to Petitioner,

Phares further discloses that Form B is made from Form A, with full conversion to Form B at ambient temperature after 7 days, 15°C after 11 days and 30°C after 1 day, suggesting stability of the treprostinil diethanolamine salt at these temperatures A POSA would . . . understand that full conversion after 7 days at ambient temperature, as disclosed by Phares, inherently teaches that Form B is stable at ambient temperature and therefore could be stored at ambient temperature.

Id. (internal citations omitted).

Patent Owner contends that Petitioner confuses “*relative* thermodynamic stabilities with actual stability.” PO Resp. 50. According to Patent Owner, “Phares provides no stability data for Form B. That one polymorph is more stable than another does not show that either is stable enough for storage in a pharmaceutical batch.” *Id.* at 50–51. We agree.

Phares teaches two crystalline forms of treprostinil diethanolamine salt, Form A and Form B. Ex. 1008, 85. Phares states that Form B appears to be “thermodynamically more stable” than the “metastable” Form A. *Id.*

at 85, 89. Phares reaches this conclusion after performing inter-conversion experiments in two different solvents, using Forms A and B material. *Id.* at 89. In isopropanol, Phares reports full conversion from Form A to Form B at ambient temperature after seven days. *Id.* Dr. Winkler testifies that this “inherently teaches that Form B is stable at ambient temperature and therefore could be stored at ambient temperature.” Ex. 1002 ¶ 203. Dr. Winkler, however, does not provide a sufficient explanation or cite any support for this conclusory statement.

Petitioner argues that “Phares discloses synthesis and isolation of treprostinil diethanolamine without specifying a temperature.” Reply 19 (citing Ex. 1008, 22). According to Dr. Winkler, “[b]ecause there is no temperature limitation here, a POSA would understand that treprostinil diethanolamine was being isolated at ambient temperature, so that it was stable at ambient temperature.” Ex. 1017 ¶ 150 (citing Ex. 2029, 249). Petitioner also argues that the fact “Phares mentions no special storage conditions for the treprostinil diethanolamine salt” further suggests nothing other than ambient temperature is required. Reply 20 (citing Ex. 1017 ¶ 153).

We are not persuaded by Dr. Winkler’s testimony or Petitioner’s arguments. As discussed above, we determine claim 6 requires actual storage, and the terms “storing”/“storage” require storing or storage for a period of at least three months. *See supra*, Section II.C.2. Even if an ordinarily skilled artisan would have understood that treprostinil diethanolamine is stable so that it can be isolated at ambient temperature, nothing in Phares suggests the salt would be stable for at least three months.

Petitioner contends the '901 patent refers to “storing” in a single sentence: “Additional advantages of this process are: (a) crude treprostinil salts can be stored as raw material at ambient temperature”¹⁸ Reply 20 (citing Ex. 1001, 17:4–6). According to Petitioner, this “confirms that a POSA would understand that all crude treprostinil salts can be stored at ambient temperature.” *Id.* “Applying the same knowledge,” Petitioner continues, “a POSA would understand the treprostinil diethanolamine salt described [in Phares] to be storable at room temperature.” *Id.* (citing Ex. 1017 ¶ 155). We are not persuaded.

An invention “must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time.” *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985). We cannot use the disclosure of the '901 patent as an instruction manual or template to supply the missing “storing”/“storage” limitation in order to piece together an obviousness theory. *See In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992).

Petitioner does not argue, let alone point to any persuasive evidence of the record to show, an ordinarily skilled artisan would have understood Phares to teach storing treprostinil diethanolamine for at least three months. Thus, we conclude Petitioner has not demonstrated by a preponderance of the evidence that the subject matter of claims 6 and 7 would have been obvious over the combination of Moriarty and Phares.

¹⁸ Elsewhere, Petitioner argues that “the '901 patent does not sufficiently describe or enable this limitation of claim 6.” Pet. 68. We do not address § 112 issues in an *inter partes* review.

F. Obviousness over Phares

Petitioner argues that claims 1–9 of the '901 patent would have been obvious over Phares. Pet. 26–48.

Because we determine that Petitioner demonstrates by a preponderance of the evidence that the subject matter of claims 1–5, 8, and 9 would have been obvious over the combination of Moriarty and Phares (*see supra*, Section II.E.1), we do not address the challenge of those claims here. *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1359 (2018) (holding a petitioner “is entitled to a final written decision addressing all of the claims it has challenged”); *Boston Sci. Scimed, Inc. v. Cook Grp. Inc.*, 809 F. App’x 984, 990 (Fed. Cir. Apr. 30, 2020) (non-precedential) (recognizing that the “Board need not address issues that are not necessary to the resolution of the proceeding” and, thus, agreeing that the Board has “discretion to decline to decide additional instituted grounds once the petitioner has prevailed on all its challenged claims”).

For claims 6 and 7, Petitioner presents the same arguments and evidence here as under the ground based on the combination of Moriarty and Phares. *Compare* Pet. 43–45, *with id.* at 68–70; *see also* Reply 26 (relying on the same arguments regarding “storing”/“storage” for both challenges). For the same reason explained above, we reject those arguments. *See supra*, Section II.E.2. Thus, we conclude Petitioner has not demonstrated by a preponderance of the evidence that the subject matter of claims 6 and 7 would have been obvious over Phares.

III. CONSTITUTIONAL CHALLENGE

Patent Owner contends subjecting the '901 patent to *inter partes* review violates its constitutional rights. PO Resp. 69–71. Patent Owner's arguments on this issue are foreclosed by the decisions in *Celgene Corp. v. Peter*, 931 F.3d 1342, 1362–63 (Fed. Cir. 2019) and *United States v. Arthrex, Inc.*, 141 S. Ct. 1970, 1986–87, 1997 (2021). As such, we do not further consider or address Patent Owner's arguments.

IV. PETITIONER'S REQUEST TO STRIKE

Petitioner seeks to strike portions of Patent Owner's Response, Sur-reply, and the Pinal Declarations (Exs. 2002, 2025). Paper 29; Exs. 1043–1046.

Petitioner's first request, related to the “not isolated” arguments, is unusual because it is prompted by Patent Owner's requested withdrawal of its own arguments. *See* Ex. 3001. We explained the situation above. *See supra*, Section II.C.3. Briefly, in its Response, Patent Owner argues “treprostinil is not isolated from the solution formed in step (b) before forming a salt in step (c).” PO Resp. 11. Later, in its Sur-reply, Patent Owner attempts to withdraw certain statements related to “not isolated” in the Response. Sur-reply 8–9; Paper 29, 1. Petitioner objected, asking us to deny this request. Ex. 3001; Tr. 16:3–5. Alternatively, Petitioner seeks to strike Patent Owner's proposed construction of step (c) in the Response and “strike all arguments in the Patent Owner Response, expert declarations (Exhibits 2002, 2025), and Sur-Reply relying on the POR's proposed construction.” Ex. 3001; Tr. 16:5–9; Paper 29, 1–2; Exs. 1043–1046.

As explained above, we determine that, in claim 1, treprostinil is not isolated from the solution formed in step (b) before forming a salt in step (c). *See supra*, Section II.C.3. Because our construction is dictated by the intrinsic evidence, and not by Patent Owner's arguments, we dismiss Patent Owner's request to withdraw its statements related to "not isolated" as moot.

Petitioner asks us to strike, in addition to the language Patent Owner seeks to withdraw, large portions of Patent Owner's Response, together with portions of Patent Owner's Response and expert declarations, because they allegedly rely on the language Patent Owner seeks to withdraw. Ex. 3001; Tr. 16:5–9; Paper 29, 1–2; Exs. 1043–1046. We deny this request.

In the Petition, Petitioner argues that an ordinarily skilled artisan "would likely understand the treprostinil acid disclosed at page 22 [of Phares] to have been isolated before addition of the base." Pet. 61. Petitioner, however, asserts that "not isolating the treprostinil before contacting it with a base is obvious based on what is taught by Phares." *Id.* In other words, Petitioner implicitly construed claim 1 to exclude an isolation step between steps (b) and (c). *See* Tr. 14:6–16:2 (maintaining that excluding isolation "is the actual right construction"). Patent Owner, thus, is entitled to respond to Petitioner's arguments on this issue, regardless of its own position on how the claim should be construed.

More importantly, we construe claim 1 to exclude isolation between steps (b) and (c). Thus, Petitioner must demonstrate the asserted prior art and the knowledge in the field teach or suggest the elimination of the isolation step, and an ordinarily skilled artisan would have had a reason to eliminate the isolation step, and would have had a reasonable expectation of success

when doing so. Petitioner cannot circumvent these requirements by striking Patent Owner’s arguments challenging, albeit unsuccessfully, Petitioner’s showing.

Petitioner also asks us to strike Patent Owner’s “Submissions Regarding ‘Storage’” in the Patent Owner Response, Sur-reply, and the two declarations of Dr. Pinal (Exs. 2002, 2025). Paper 29, 8. According to Petitioner, Patent Owner’s expert in the parallel district court case, Dr. Robert R. Ruffolo, testified that, in the ’901 patent, actual storage was not required. *Id.* at 3–5 (citing Ex. 2034, 130:12–132:4, 132:15–136:11). This is inconsistent, Petitioner asserts, with Patent Owner’s position in this proceeding. *Id.* at 2. Even though Petitioner is correct on this point, we decline to strike Patent Owner’s arguments related to “storage.”

As explained above, we determine claim 6, by explicitly reciting “storing,” requires actual storage. *See supra*, Section II.C.2. An expert’s testimony, clearly at odds with the unambiguous claim language, does not absolve Petitioner of its burden to demonstrate that the prior art teaches or suggests this limitation.

In sum, in view of our construction of step (c) and the terms “storing”/“storage” based on the intrinsic evidence, we deny Petitioner’s Request to Strike.

V. PATENT OWNER’S MOTION TO EXCLUDE

Patent Owner filed a Motion to Exclude Exhibits 1002 and 1012, as well as the portions of the Petition and Reply that rely on these exhibits. Paper 31, 2. For the reasons provided below, we deny Patent Owner’s Motion to Exclude.

A. Winkler Declaration (Ex. 1002)

Petitioner relies on the Winkler Declaration (Ex. 1002) to support the arguments in the Petition. Pet. 3. Patent Owner contends that Exhibit 1002 “purports to be a declaration, but without authentication because it lacks the statutorily-required oath or caveat for a declaration.” Paper 31, 3 (citing 35 U.S.C. § 25; 37 C.F.R. § 42.2). Alternatively, Patent Owner asserts that “Prof. Winkler’s declaration warrants no weight because it lacks the required oath or perjury statement.” PO Resp. 17 (citing 35 U.S.C. § 25(b); 37 C.F.R. § 42.63).

Under our Rules, “[e]vidence consists of affidavits, transcripts of depositions, documents, and things” (37 C.F.R. § 42.63(a)), and “[u]ncompelled direct testimony must be submitted in the form of an affidavit” (*id.* § 42.53(a)). “*Affidavit* means affidavit or declaration under [37 C.F.R.] § 1.68 [A] declaration under 28 U.S.C. 1746 may be used as an affidavit.” *Id.* § 42.2.

As Patent Owner correctly points out, Exhibit 1002, the purported declaration of Dr. Winkler, “does not state that the testimony is true or believed to be true, much less reference the penalty for making willful false statements.” PO Resp. 18.

Petitioner does not dispute this deficiency. Instead, Petitioner argues that Patent Owner “waived its argument regarding Dr. Winkler’s declaration under 37 C.F.R. § 42.63, because it did not timely object to the issue with sufficient particularity . . . to allow correction in the form of supplemental evidence.” Paper 32, 1 (internal quotation marks omitted). We disagree with Petitioner.

First, “[a]ny objection to evidence submitted during a preliminary proceeding must be filed within ten business days of the institution of the trial.” 37 C.F.R. § 42.64(b)(1). We instituted trial on October 13, 2020; and Patent Owner timely filed and served its objections to Exhibit 1002 on October 27, 2020. *See* Paper 10.

Second, “[a] motion to exclude evidence must be filed to preserve any objection.” 37 U.S.C. § 42.64(c). Patent Owner timely filed a Motion to Exclude Exhibit 1002 (Paper 31, 2), and thus, has properly preserved its objections to Exhibit 1002.

Third, Petitioner faults Patent Owner for, in the objections, “generically restat[ing] FRE 802, 901, and 902, and never identified the oath as the issue.” Paper 32, 1; *see also* Tr. 21:19 (“The objections weren’t specific to the perjury statement.”); *id.* at 23:2–4 (arguing that Patent Owner’s objection was “ambiguous”). We disagree.

Patent Owner objected to Exhibit 1002 “under FRE 901-902 as lacking authentication and not self-authenticating because it lacks sufficient indicia that the exhibit is what it purports to be.” Paper 10, 3. According to Patent Owner, Petitioner “does not state that it did not understand the objection . . . , that it sought clarification from [Patent Owner], or that it could not identify how the exhibit lacked authentication.” Paper 37, 1.

During oral argument, Petitioner explained that “we didn’t realize that it was the perjury statement in particular that they were referring to. Or, we didn’t realize that it had been omitted. And so, we looked at the signature and saw that it was there.” Tr. 22:1–4; *see also id.* at 23:3–6 (“[W]hen we saw a lack of authentication [objection], we thought, oh, did Dr. Winkler not

sign his declaration. We saw that it was signed. We did not realize that they were actually referring to the perjury statement.”).

Counsel for Patent Owner pointed out, and Petitioner did not dispute, “if it’s a declaration, the only thing that would render it inauthentic would be the lack of a signature or an oath[; those] are the only two things it could possibly be.” Tr. 40:3–5. We find Patent Owner’s objection sufficient to put Petitioner on notice that the authentication of Exhibit 1002 is problematic; no more is required of Patent Owner. The fact that Petitioner did not realize the authentication objection is directed to the lack of perjury statement, instead of the lack of a signature, does not make Patent Owner’s objection ambiguous. Thus, we conclude that Patent Owner has not waived its argument regarding Dr. Winkler’s declaration under 37 C.F.R. § 42.63.

Petitioner argues that “any omissions in Dr. Winkler’s declaration with respect to the oath or perjury statement were harmless and have been cured.” Paper 32, 2; Reply 1–2. Petitioner points out that (1) Patent Owner deposed Dr. Winkler on his opinions in Exhibit 1002; and (2) Dr. Winkler “refiled Ex. 1002 as Ex. 1039” and Patent Owner “has not moved to exclude Ex. 1039 or any [of] Dr. Winkler’s opinions therein.” Paper 32, 2; Reply 2. According to Petitioner, Patent Owner “is exalting form over substance in renewing this objection.” Paper 32, 2. We reject Petitioner’s cavalier attitude towards this matter.

First, because Exhibit 1039 was filed without proper authorization, we give it no weight in rendering this Decision. Exhibit 1039 is not a declaration in support of the Reply; instead, it was a “[r]efiled Declaration of Jeffrey D. Winkler, Ph.D. (Ex. 1002)” that is in support of the Petition.

Paper 42, 4; Ex. 1039, cover page. But, the Petition was filed on March 30, 2020 (Pet. 76; Paper 3, 1), and Exhibit 1039 was filed on March 1, 2021 (Ex. 1039, 81). Petitioner does not explain how a declaration executed eleven months after can support the Petition.

Exhibit 1039 is not proper supplemental evidence either. Under 37 C.F.R. § 42.64(b)(2), “[t]he party relying on evidence to which an objection is timely served may respond to the objection by serving supplemental evidence within ten business days of service of the objection.” During oral argument, counsel for Patent Owner represented, and counsel for Petitioner did not dispute, that Petitioner served Exhibit 1039 on the same day it filed the Reply. Tr. 39:5–23. That is more than four months after Patent Owner timely served the objections to Exhibit 1002. Thus, Exhibit 1039 is not proper supplemental evidence in response to Patent Owner’s objection. *See* Paper 31, 2 (“No supplemental evidence was timely filed to address the[] objections.”).

Second, Petitioner relies on *Google LLC v. CyWee Group Ltd.*, IPR2018-01257, Paper 69 (PTAB Sept. 6, 2019), and *Fidelity Information Services, LLC v. Mirror Imaging, LLC*, CBM2017-00064, Paper 54 (January 2, 2019). Paper 32, 2. As Petitioner recognizes, in those two cases, the Board “grant[ed] party *authorization to correct* unsworn declaration when opposing party cross-examined the expert.” *Id.* (emphasis added). What is critically missing here, however, is that Petitioner never sought leave to correct the unsworn declaration. In fact, Petitioner never brought the issue to the attention of the Board. Instead, it resorted to self-help and “fixed” the issue through a filing without authorization. *See* Tr. 22:5–7.

Despite our concerns over Petitioner first submitting a defective “declaration,” and then disregarding our Rules when attempting to correct the mistake, we find Patent Owner has suffered no undue prejudice. As Petitioner emphasizes, Patent Owner deposed Dr. Winkler on his opinions in Exhibit 1002. Paper 32, 2 (citing Ex. 2026). Indeed, Patent Owner’s counsel conceded so during the oral argument. Tr. 64:5–6 (“I’d be hard pressed to sit here and say . . . that we suffered a specific cognizable prejudice.”). As a result, we deny Patent Owner’s Motion to Exclude Exhibit 1002.

B. Kawakami (Ex. 1012)

Patent Owner also seeks to exclude Kawakami because, although it purports to be a translation of JP56-122328, it is not authenticated, and not a verified translation. Paper 31, 2, 10–11.

Patent Owner points out that Exhibit 1012 “contains neither the purported Japanese document being translated, nor a verified translator’s declaration.” *Id.* at 10. Patent Owner states that it “timely objected to EX1012 under FRE 402, 403, 802, 803-807, 901, 902, 1001-1003, 1012,” but Petitioner failed to timely serve any supplemental evidence to address these objections. *Id.* at 3 (citing Paper 10, 2–3). Patent Owner also contends that Petitioner has failed to comply with 37 C.F.R. § 42.63(b). *Id.* at 11; *see also* 37 C.F.R. § 42.63(b) (requiring the party who relies on a document in a foreign language to file, with the original document, an English translation, and an affidavit attesting to the accuracy of the translation).

Petitioner argues “Ex. 1012 is exactly the same Kawakami document that was submitted in the IPR2016-00006 as Ex. 1007.” Paper 32, 7. Together with its Opposition to Patent Owner’s Motion to Exclude,

Petitioner submitted Exhibits 1047–1051, which are “the original Japanese version of Kawakami and declarations attesting to and confirming the accuracy of the translation,” originally filed as Exhibits 1006, 1007, 1011, 1019, and 1020 in IPR2016-00006. *Id.* at 8. According to Petitioner, “[t]he filing of these exhibits remedies any failure to comply with § 42.63(b) or FRE 902(3), which in any event is harmless error.”

As with Petitioner’s omission and later self-help relating to Exhibit 1002, we do not condone Petitioner’s omission and self-help here either. Petitioner contends that Patent Owner “did not move to exclude the identical Kawakami translation in IPR2016-00006, and the Board [in that case] relied on the same translation for an entire ground in its final written decision.” Paper 32, 7. Petitioner fails to recognize that the petitioner in that case properly complied with our Rules, and there was no good-faith basis for Patent Owner to seek any exclusion.

Despite our disappointment over Petitioner’s repeated carelessness, we deny Patent Owner’s Motion to Exclude Exhibit 1012. First, Petitioner relies on Exhibit 1012 through Dr. Winkler’s testimony. Pet. 23–24 (citing Ex. 1002 ¶ 49), 55 (citing Ex. 1002 ¶ 157). Under Federal Rules of Evidence 703, Dr. Winkler may rely on facts or data that are not admissible themselves.

Second, “a comparison between the IPR copies of a reference and a version of the reference proven to be prior art was evidence that the IPR reference was prior art.” *Valve Corp. v. Ironburg Inventions Ltd.*, 8 F.4th 1364, 1371 (Fed. Cir. 2021) (citing *VidStream LLC v. Twitter, Inc.*, 981 F.3d 1060, 1066–67 (Fed. Cir. 2020)). In the ’393 Decision, the panel

relied on Kawakami in analyzing one of the obviousness grounds. *See* the '393 Dec. 68–84. Kawakami was properly authenticated in that proceeding. *See* IPR2016-00006, Exs. 1006, 1007, 1011, 1019, 1020. Because a comparison shows Exhibit 1012 in this case is the same as Exhibit 1007 in IPR2016-00006, we deny Patent Owner's Motion to Exclude Exhibit 1012.

VI. PETITIONER'S MOTION TO SUBMIT SUPPLEMENTAL INFORMATION

Under our Rules,

A party seeking to submit supplemental information more than one month after the date the trial is instituted, must request authorization to file a motion to submit the information. The motion to submit supplemental information must show why the supplemental information reasonably could not have been obtained earlier, and that consideration of the supplemental information would be in the interests-of-justice.

37 C.F.R. § 42.123(b).

With our authorization, Petitioner filed a Motion, seeking to submit the Claim Construction Order from the parallel district court case. Paper 38, 1. At the time of the Motion, only the Proposed Order was available. Ex. 1054. Patent Owner does not oppose the Motion in this respect, and submitted the official Order as Exhibit 2035. Paper 40, 2. Patent Owner represents that Petitioner consented to this submission. *Id.*

Our Rules require that we consider “[a]ny prior claim construction determination concerning a term of the claim in a civil action . . . that is timely made of record in the *inter partes* review proceeding.” 37 C.F.R. § 42.100(b). The parties timely filed the Claim Construction Order before

the oral hearing in this proceeding. *See* Paper 38, 2–3 (arguing the *Markman* Order could not have been obtained earlier). Thus, Petitioner’s Motion to submit the Claim Construction Order from the district court case is granted, and Exhibit 2035 is admitted into evidence in this proceeding.¹⁹

Petitioner also seeks to submit the transcript from the *Markman* hearing at the district court (Ex. 1054). Paper 38, 1. According to Petitioner, “the hearing transcript contains further evidence of Patent Owner’s inconsistencies in its claim construction positions between the tribunals, and the district court’s evaluation of those inconsistencies as likely disclaimer.” *Id.* at 5; *see also id.* at 6–8 (listing “relevant excerpts”).

Patent Owner opposes the Motion in this respect. Paper 40, 2. According to Patent Owner, many of Petitioner’s citations to the hearing transcript “amount to attempts to supplement the record with its own further attorney argument and engage in a game of gotcha regarding allegedly inconsistent statements.” *Id.* at 2–3.

Because we consider the Claim Construction Order from the district court, and because the *Markman* hearing transcript helps to explain how the district court came to its constructions in the Order, we find it is in the interests of justice to admit the hearing transcript into evidence of the record in this proceeding, for just that purpose.

In sum, Petitioner’s Motion to Submit Supplemental Information is granted.

¹⁹ Because Exhibit 1054 is superseded, we expunge it from the record.

VII. CONCLUSION²⁰

After reviewing the entire record and weighing evidence offered by both parties, we determine that (1) Petitioner has demonstrated by a preponderance of the evidence that claims 1–5, 8, and 9 of the '901 patent would have been obvious over the combination of Moriarty and Phares; and (2) Petitioner has not demonstrated by a preponderance of the evidence that claims 6 and 7 of the '901 patent would have been obvious over either Phares alone, or the combination of Moriarty and Phares.

In summary:

Claims	35 U.S.C. §	Reference(s)	Claims Shown Unpatentable	Claims Not shown Unpatentable
1–9	103	Moriarty, Phares	1–5, 8, 9	6, 7
1–9	103	Phares		6, 7
Overall Outcome			1–5, 8, 9	6, 7

²⁰ Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. See 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. See 37 C.F.R. § 42.8(a)(3), (b)(2).

VIII. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has demonstrated by a preponderance of the evidence that claims 1–5, 8, and 9 are unpatentable;

FURTHER ORDERED that Petitioner has not demonstrated by a preponderance of the evidence that claims 6 and 7 are unpatentable;

FURTHER ORDERED that Petitioner’s Request to Strike (Paper 29) is denied;

FURTHER ORDERED that Patent Owner’s Motion to Exclude (Paper 31) is denied;

FURTHER ORDERED that Petitioner’s Motion to Submit Supplemental Information (Paper 38) is granted; and

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

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