No. 23-___

IN THE

Supreme Court of the United States

LIQUIDIA TECHNOLOGIES, INC.,

Petitioner,

v.

UNITED THERAPEUTICS CORPORATION,

Respondent.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTORIARI

SANYA SUKDUANG
COOLEY LLP
1299 Pennsylvania Ave.
Suite 700
Washington, DC 20004
(202) 842-7800

KATHLEEN R. HARTNETT
Counsel of Record
COOLEY LLP
3 Embarcadero Center,
20th Floor
San Francisco, CA 94111
(415) 693-2000
khartnett@cooley.com

PATRICK J. HAYDEN
COOLEY LLP
55 Hudson Yards
New York, NY 10001
(212) 479-6000

ADAM S. GERSHENSON
ALEX ROBLEDO
COOLEY LLP
500 Boylston Street
Boston, MA 02116
(617) 937-2300

Counsel for Petitioner Liquidia Technologies, Inc.

January 23, 2024

WILSON-EPES PRINTING CO., INC. – (202) 789-0096 – WASHINGTON, D.C. 20002

QUESTIONS PRESENTED

Under the Leahy-Smith America Invents Act ("AIA"), a party may challenge the validity of a patent in an *inter partes* review proceeding before the Patent Trial and Appeal Board ("PTAB") and obtain a decision regarding the patent's validity. In this case, the PTAB issued a final written decision holding that a patent held by Respondent United Therapeutics, Inc. ("UTC") was invalid. Subsequently, however, the Federal Circuit held that Petitioner Liquidia Technologies, Inc. ("Liquidia") was liable for induced infringement of the same patent, notwithstanding the PTAB's invalidity determination. In the Federal Circuit's view, the PTAB's decision had "no impact" on this infringement litigation, primarily because the PTAB's decision was pending on appeal.

The questions presented are:

1. Whether a party may be liable for induced patent infringement when the PTAB has already issued a final written decision determining that the same patent is invalid.

2. Whether a final written decision of the PTAB remains preclusive while it is pending on appeal.

PARTIES TO THE PROCEEDING

Petitioner Liquidia Technologies, Inc. was defendant in the district court and appellant before the court of appeals. Respondent United Therapeutics Corp. was plaintiff in the district court and appellee and cross-appellant before the court of appeals.

STATEMENT OF RELATED CASES

The following proceedings are directly related to this case within the meaning of Rule 14.1(b)(iii):

- *United Therapeutics Corp. v. Liquidia Technologies, Inc.*, Nos. 2022-2217, 2023-1021 (Fed. Cir.), judgment entered on July 24, 2023; and
- *United Therapeutics Corp. v. Liquidia Technologies, Inc.*, No. 1:20-cv-00755-RGA (D. Del.), judgment entered on September 9, 2022.

CORPORATE DISCLOSURE STATEMENT

Petitioner Liquidia Technologies, Inc. is a wholly owned subsidiary of Liquidia Corporation, which is a publicly held corporation.

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

Cases

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

TABLE OF AUTHORITIES
(continued)

Page(s)

Statutes

TABLE OF AUTHORITIES
(continued)

Page(s)

Regulations

Legislative Materials

TABLE OF AUTHORITIES
(continued)

Page(s)

Other Authorities

TABLE OF AUTHORITIES
(continued)

Page(s)

PETITION FOR WRIT OF CERTIORARI

Liquidia Technologies, Inc. petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The Federal Circuit's decision affirming the district court's judgment (Pet. App. 1a–25a) is reported at 74 F.4th 1360 (Fed. Cir. 2023). The Federal Circuit's order denying Liquidia's petition for rehearing en banc (Pet. App. 92a–93a) is unreported. The district court's opinion (Pet. App. 29a–91a) is reported at 624 F. Supp. 3d 436 (D. Del. 2022). The district court's final judgment (Pet. App. 26a–28a) is unreported.

JURISDICTION

The Federal Circuit entered judgment on July 24, 2023 and denied rehearing on September 26, 2023. Chief Justice Roberts extended the time to file this petition to January 24, 2024. This Court has jurisdiction under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

The relevant statutory provisions are reproduced in the Appendix to this petition (Pet. App. 162a–172a).

INTRODUCTION

This case concerns whether a decision by the Patent Trial and Appeal Board determining that a patent is invalid is preclusive in patent infringement litigation between the parties. Under this Court's precedent, the answer should have been an easy yes: it has long been settled that an invalid patent cannot be infringed, and that a determination of patent invalidity before one tribunal precludes subsequent liability for infringement before another.

In a pair of decisions in 2015, this Court confirmed that preclusion works precisely this way when, as here, the determination of invalidity has been made by the PTAB. First, in *Commil USA, LLC v. Cisco Systems, Inc.*, 575 U.S. 632 (2015), the Court held that "accused inducers who believe a patent is invalid" are "immune from liability" for induced infringement if they successfully "seek *inter partes* review at the [PTAB] and receive a decision as to validity within 12 to 18 months." *Id.* at 645 (citing 35 U.S.C. § 316). And in *B & B Hardware Inc. v. Hargis Industries, Inc.*, 575 U.S. 138 (2015), the Court held that the determinations by the Trademark Trial and Appeal Board ("TTAB")—PTAB's sister agency within the U.S. Patent and Trademark Office ("PTO")—are preclusive in trademark infringement litigation. *Id.* at 151. Together, these rulings make clear that a party may defeat liability for patent infringement by obtaining a PTAB decision determining that the patent at issue is invalid.

Petitioner Liquidia Technologies, Inc. did exactly as this Court instructed. After Respondent United Therapeutics, Inc. sued Liquidia for induced infringement, Liquidia petitioned the PTAB for *inter partes* review of the patent at issue, and the PTAB issued a final written decision, prior to resolution of the parallel district court litigation on the same patent, holding that UTC's patent claims at issue were invalid. That should have been dispositive in this case: under *Commil* and *B & B Hardware*, the PTAB's determination that UTC's patent claims are invalid meant that Liquidia could not be liable for induced infringement of that patent.

The Federal Circuit failed to follow this Court's command, however, and affirmed judgment against

Liquidia for induced infringement of UTC's patent—despite the PTAB's invalidity determination. According to the Federal Circuit, because the PTAB's decision was pending on appeal, it was "non-final" and entitled to no preclusive effect at all. Pet. App. 20a. That conclusion is plainly wrong. As this Court and every single circuit has held, it is hornbook law that a decision remains preclusive while on appeal. *See* 18A C. Wright, A. Miller & E. Cooper, *Federal Practice and Procedure* § 4433 (3d ed., Supp. 2023) ("The Supreme Court long ago seemed to establish the rule that a final judgment retains all of its res judicata consequences pending decision of the appeal," and "[t]he lower courts have taken the rule as settled ever since."); Restatement (Second) of Judgments § 13, cmt. f (1982) ("[A] judgment otherwise final remains so despite the taking of an appeal"). The Federal Circuit's contrary holding here conflicts with this Court's precedents, the decisions of every circuit, and the basic preclusion principles this Court has long demanded that courts apply to agency decisions like those of the PTAB.

The consequences of the Federal Circuit's ruling are grave. With respect to patent law, the decision destabilizes the *inter partes* review process, which Congress designed to make patent litigation more efficient and less expensive by providing a straightforward mechanism for obtaining validity determinations that bar or at least streamline infringement litigation. Under the Federal Circuit's framework, however, parties may now simply disregard the PTAB's determinations of invalidity and pursue costly infringement litigation anyway, so long as an appeal—no matter its merits—is on the books.

Moreover, the harmful consequences of the Federal Circuit's ruling are not limited to patent law.

Its holding that an agency's decision has no preclusive effect while on appeal is not patent-specific and threatens to undermine fundamental principles of preclusion more generally. Under the Federal Circuit's reasoning, a party may simply ignore an adverse agency decision by lodging an appeal of that decision and then pursuing litigation clearly barred by the prior ruling. On the flip side, under the Federal Circuit's approach, a party who prevails before an agency *must* litigate any appeal filed—and obtain affirmance—if it wants its win to mean anything in future litigation. That is not how the law of preclusion works, which is why this Court and every circuit has rejected it.

Finally, this case provides the right vehicle for resolving the questions presented. The Federal Circuit's holding was unequivocal: a PTAB determination of invalidity has "no impact" on patent infringement litigation unless and until it has been affirmed on appeal, and the existence of an appeal alone defeats preclusion. The Federal Circuit provided no caveats and denied rehearing en banc, thus committing itself to an anomalous rule that clearly conflicts with the precedent of this Court, every single circuit, and settled preclusion law.

This Court should grant the petition for a writ of certiorari.

STATEMENT OF THE CASE

A. Statutory Framework

"From their inception, the federal patent laws have embodied a careful balance between the need to promote innovation and the recognition that imitation and refinement through imitation are both necessary to invention itself and the very lifeblood of a

competitive economy." *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146 (1989). Accordingly, for decades, Congress has authorized the U.S. Patent and Trademark Office to "reexamine—and perhaps cancel—a patent claim that it had previously allowed" through various types of administrative review proceedings. *Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 267 (2016).

In 2011, Congress overhauled the patent system, including its reexamination mechanisms, when it passed the Leahy-Smith America Invents Act ("AIA"). Pub. L. 112-29, 125 Stat. 284 (2011). Among other things, the AIA created the Patent Trial and Appeal Board, which consists of experienced patent attorneys, and tasked it with overseeing three new types of administrative proceedings to review the validity of patents after they have been issued. *See Return Mail, Inc. v. United States Postal Serv.*, 139 S. Ct. 1853, 1860 (2019).

One of these proceedings is known as *inter partes* review ("IPR"). IPR is a process that permits "a person," other than the patent owner, to petition for the review of a patent on the ground that one or more of its claims is unpatentable, either because the claim lacks "novelty" or because the claim is "obvious" in light of "patents or printed publications" existing at the time of the patent application. 35 U.S.C. § 311(a)–(b); *see id.* §§ 102–03. In creating IPR as a means of challenging the validity of patents post-issuance, Congress sought to "establish a more efficient and streamlined patent system that will improve patent quality and limit unnecessary and counterproductive litigation costs." H.R. Rep. 112-98, pt. 1, at 40 (2011).

After an IPR petition is filed, the PTO Director determines whether an IPR should be instituted,

based on whether the petition presents "a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). An IPR proceeding, which is overseen by PTAB, *see* 35 U.S.C. § 316(c), is an "adjudicatory" review proceeding that involves discovery, affidavits and other written memoranda, and an oral hearing, *see Return Mail*, 139 S. Ct. at 1860 (citing 35 U.S.C. § 316).

After receiving and reviewing the evidence, the PTAB issues a "Final Written Decision" with respect to the patentability of any challenged patent claim. *Id.* § 318(a). The PTAB must issue its decision no later than 12–18 months after the institution of IPR proceedings. *Id.* § 316(a)(11).[1]

For IPR petitioners who obtain such a final written decision, the AIA contains two "estoppel" provisions. First, the petitioner "may not request or maintain a proceeding" before the PTO "with respect to [the patent] claim on any ground that the petitioner raised or reasonably could have raised" during the IPR. 35 U.S.C. § 315(e)(1). Second, the petitioner may not, in civil litigation, assert that the patent claim "is invalid on any ground that the petitioner raised or reasonably could have raised during the inter partes review." *Id.* § 315(e)(2). Once instituted, in other words, the IPR is intended to conclusively determine questions of patent invalidity.

---

[1] The AIA provides that PTAB's final written decision must issue "not later than 1 year after" the PTO institutes IPR proceedings, though the PTO Director may, upon "good cause shown, extend the 1-year period by not more than 6 months." 35 U.S.C. § 316(a)(11). Thus, a final written decision must issue within 12–18 months.

A party dissatisfied with a final written decision may either seek panel rehearing of the decision before the PTAB within 30 days, *see* 37 C.F.R. § 42.71(d)(2), and/or appeal the decision to the Federal Circuit, *see* 35 U.S.C. §§ 319, 141(c). Upon the issuance of a final written decision by the PTAB and the expiration or termination of any appeal, the PTO Director "shall issue and publish a certificate" confirming or canceling any or all of the challenged patent claims in accordance with the decision. 35 U.S.C. § 318(b).

B. Factual Background

This case concerns Liquidia's YUTREPIA™ product, a dry powder inhalation formulation of a drug compound called treprostinil, developed to treat pulmonary arterial hypertension ("PAH"). PAH is a chronic, potentially life-threatening health condition that is characterized by elevated blood pressure in the lungs. Pet. App. 2a. Treprostinil is used to treat PAH because it is a vasodilator that can dilate (open) precapillary blood vessels, which in turn can reduce blood pressure. Pet. App. 2a. In January 2020, Liquidia filed a New Drug Application ("NDA") for YUTREPIA™, a first-of-its kind powder formulation of treprostinil that is easier to use than other PAH drugs, leading to improved patient compliance and disease outcomes. Pet. App. 3a–4a, 113a.

After Liquidia filed its NDA, Respondent UTC filed a patent application that eventually issued as U.S. Patent 10,716,793 ("the '793 patent") on July 21, 2020. Pet. App. 4a, 97a. The '793 patent is directed to "a method of treating [PAH] comprising inhalation of treprostinil." Pet. App. 4a–5a. UTC holds an NDA for Tyvaso®, an inhaled solution formulation of treprostinil approved to treat PAH. Pet. App. 2a.

C. Procedural History

The parties' dispute involves both the patent infringement action that is the subject of this petition and a parallel *inter partes* review for the '793 patent.

1. UTC Sues Liquidia for Infringement

In June 2020, UTC sued Liquidia in the U.S. District Court for the District of Delaware, alleging that Liquidia's YUTREPIA™ product infringed or induced infringement of various patents UTC owns, including the '793 patent. Pet. App. 2a. In March 2022, the district court conducted a bench trial, during which Liquidia presented non-infringement and validity defenses with respect to the '793 patent. Pet. App. 30a.

2. Liquidia Obtains a Final Written Decision of Invalidity from the PTAB

While the infringement litigation was pending in the district court, Liquidia filed with the PTO a petition for *inter partes* review of the '793 patent, alleging that all claims of the '793 patent were unpatentable or invalid as obvious over prior art at the time of invention. Pet. App. 4a.

On July 19, 2022—before the district court issued its post-trial opinion in the infringement litigation—the PTAB issued a final written decision regarding the '793 patent, which considered extensive written discovery and determined that all claims of the '793 patent were unpatentable as obvious over prior art. Pet. App. 4a, 94a–143a. UTC requested rehearing of PTAB's final written decision, which PTAB denied. Pet. App. 144a–161a. In its rehearing decision, the PTAB again determined that all claims of the '793 patent were unpatentable as obvious. Pet. App. 4a,

157a–159a. UTC then appealed the PTAB's final written decision to the Federal Circuit. Pet. App. 4a.

3. The District Court Finds Induced Infringement Despite the PTAB's Final Written Decision of Invalidity

On July 19, 2022—the same day the PTAB issued its final written decision—Liquidia submitted that decision to the district court, which had not yet issued a post-trial opinion. Dkt. No. 425. The district court requested briefing to address the issue of whether PTAB's final written decision "compels that [the district court] treat the '793 patent as being invalid," Dkt. No. 426, which the parties then submitted.

On August 31, 2022, the district court issued its post-trial opinion, concluding, *inter alia*, that all asserted claims of the '793 patent were valid and that Liquidia induced infringement of the '793 patent. Pet. App. 5a–7a, 90a–91a. The district court refused to give the PTAB's decision preclusive effect, claiming that the decision "does not have collateral estoppel effect until that decision is affirmed or the parties waive their appeal rights." Pet. App. 70a.

4. The Federal Circuit Affirms the District Court's Finding of Induced Infringement

On appeal, Liquidia argued that it could not be held liable for induced infringement of the '793 patent because the PTAB had already found the patent unpatentable in an IPR. Pet. App. 19a. In response, UTC argued that PTAB's final written decision was not "final" for preclusion purposes and thus did not defeat Liquidia's liability for inducing infringement. Pet. App. 19a–20a.

The Federal Circuit affirmed the district court's finding that Liquidia was liable for inducing infringement. Pet. App. 20a–21a. Like the district court, the Federal Circuit refused to accord preclusive effect to the PTAB's determination of invalidity, holding that because UTC's appeal of the PTAB's determination was pending, the agency's decision was "[a] pending, non-final litigation" which "does not have collateral estoppel effect until that decision is affirmed or the parties waive their appeal rights." Pet. App. 20a (citing *XY, LLC v. Trans Ova Genetics, L.C.*, 890 F.3d 1282, 1294 (Fed. Cir. 2018)). The Federal Circuit also noted that the PTAB's final written decision "does not cancel claims." Pet. App. 20a (citing 35 U.S.C. § 318(b)). According to the Federal Circuit, "[t]he '793 IPR decision thus has no impact here on a finding of induced infringement." Pet. App. 20a–21a.

The Federal Circuit denied both Liquidia's and UTC's petitions for rehearing en banc. Pet. App. 92a–93a.

5. The Federal Circuit Affirms the PTAB's Final Written Decision

On December 20, 2023, the Federal Circuit affirmed the PTAB's final written decision concluding that all claims of the '793 patent are unpatentable. *United Therapeutics Corp. v. Liquidia Techs., Inc.*, No. 2023-1805, 2023 WL 8794633 (Fed. Cir. Dec. 20, 2023).

REASONS FOR GRANTING THE WRIT

In two related ways, the Federal Circuit's decision in this case conflicts with the decisions of this Court, those of other circuits, and the hornbook preclusion law these courts apply. First, the Federal Circuit contradicted this Court's clear holdings that the PTAB's final written decision of patent invalidity is

preclusive in later infringement litigation. Second, the Federal Circuit's holding that the pendency of an appeal strips a PTAB decision of its preclusive effect conflicts with the preclusion law precedent of this Court and every single circuit. These issues are undeniably important, as the Federal Circuit's ruling jeopardizes the functioning of the PTAB, whose IPR invalidity decisions now may be rendered immediately toothless simply by the filing of an appeal. The Federal Circuit also has created an unfounded exception to preclusion law, which may erase the effect of *any* decision (whether of a court or agency) so long as an appeal is lodged. This Court's review is urgently required.

I. The Federal Circuit's Decision Disregards This Court's Decisions in *Commil* and *B & B Hardware*

Whether the PTAB's final written decision precluded Liquidia's liability for induced infringement did not present the Federal Circuit with a novel question. To the contrary, in 2015, this Court—building upon decades of its own precedent—made clear that a final written decision by the PTAB regarding patent invalidity is binding in patent infringement litigation. The Federal Circuit's conclusion that the PTAB's final written decision nonetheless has "no impact" in this infringement litigation violates this Court's precedent—on an issue over which it has virtually exclusive jurisdiction among the courts of appeals—and warrants review.

1. It is settled law that a determination of patent invalidity precludes a claim of patent infringement. In *Blonder-Tongue Laboratories, Inc. v. University of Illinois Foundation*, 402 U.S. 313 (1971), the Court

overturned its earlier precedent and held that issue preclusion (collateral estoppel) applies where a party "fac[es] a charge of infringement of a patent that has once been declared invalid." *Id.* at 350. *Blonder-Tongue* recognized that "[p]ermitting repeated litigation" was both wasteful and unfair—it would divert a defendant's "time and money … to relitigation of a decided issue" and would reflect "the aura of the gaming table." *Id.* at 329.

Blonder-Tongue's preclusion principle has governed patent infringement litigation ever since. *See, e.g.*, *MaxLinear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1376 (Fed. Cir. 2018) ("[A]s a result of collateral estoppel, a judgment of invalidity in one patent action renders the patent invalid in any later actions based on the same patent." (quotations and citation omitted)); *Mendenhall v. Barber-Greene Co.*, 26 F.3d 1573, 1577 (Fed. Cir. 1994) ("[O]nce the claims of a patent are held invalid in a suit involving one alleged infringer, an unrelated party who is sued for infringement of those claims may reap the benefit of the invalidity decision under principles of collateral estoppel." (citing *Blonder–Tongue*, 402 U.S. 313)).

2. In *Commil USA, LLC v. Cisco Systems, Inc.*, 575 U.S. 632 (2015), this Court confirmed that this principle applies to patent invalidity determinations by the PTAB following *inter partes* review. *Commil* held that a defendant's subjective "belief regarding patent validity" is not "a defense to a claim of induced infringement." *Id.* at 642. However, it also recognized that if "an act that would have been an infringement or an inducement to infringe pertains to a patent that is shown to be invalid, there is no patent to be infringed." *Id.* at 644; *see also id.* at 648 (Scalia, J.,

dissenting on other grounds) ("To talk of infringing an invalid patent is to talk nonsense.").

Commil then held what is dispositive here: "accused inducers who believe a patent is invalid have various proper ways to obtain a ruling to that effect," including by "seek[ing] *inter partes* review at the Patent Trial and Appeal Board and receiv[ing] a decision as to validity within 12 to 18 months." *Id.* at 645 (citing 35 U.S.C. § 316). "If the defendant is successful," the Court held, "he will be immune from liability." *Id.* Liquidia followed precisely this path here: it sought PTAB review of UTC's patent, and it received a determination of invalidity from the PTAB before the district court ruled on UTC's claim of induced infringement. That should have precluded Liquidia's liability for induced infringement.[2]

Commil's holding is expressly grounded in the PTAB's statutory framework. *Commil* relied upon 35 U.S.C. § 316, which outlines the IPR process and requires, *inter alia*, that an IPR conclude within 1 year, a period that is extendable to 6 months with good cause. *See* 35 U.S.C. § 316(a)(11). Thus, as *Commil* recognized, if the 12-to-18 month IPR process—and

---

[2] The final written decision's determination that the patent claims at issue are "unpatentable" is synonymous with a determination that the patent is "invalid." Indeed, referring to the applicable statutory framework, *Commil* stated that "parties can seek *inter partes* review at the Patent Trial and Appeal Board and receive a decision as to *validity* within 12 to 18 months." *Commil*, 575 U.S. at 645 (emphasis added) (quoting 35 U.S.C. § 316); *see also* E. Surette, Annotation, *Motions to Lift or Continue Stay of Patent Litigation Pending Inter Partes Review*, 29 A.L.R. Fed. 3d art. 9 (2018) ("It should be noted that IPR addresses only invalidity, not infringement.").

the IPR process *only*—results in a determination of patent invalidity, that determination alone precludes liability for patent infringement.

3. The same term as *Commil*, in *B & B Hardware Inc. v. Hargis Industries, Inc.*, 575 U.S. 138 (2015), this Court confirmed that the fundamentals of issue preclusion law compel this result. *B & B Hardware* held that a decision by the TTAB—PTAB's sister agency within the PTO—regarding likelihood of confusion is preclusive in later district court trademark infringement litigation. *Id.* at 141–42. As the Court explained, its "cases and the Restatement make clear that issue preclusion is not limited to those situations in which the same issue is before two *courts*," and "where a single issue is before a court and an administrative agency, preclusion also often applies." *Id.* at 148.

Thus, "courts may take it as given that Congress has legislated with the expectation that the principle of issue preclusion will apply except when a statutory purpose to the contrary is evident"—just as the Court itself did in *Commil*. *Id.* (citation and alterations omitted). And the Court readily rejected the argument that the mere availability of judicial review of a TTAB decision in federal court meant the agency's decisions were not preclusive, as "[o]rdinary preclusion law teaches that if a party to a court proceeding does not challenge an adverse decision, that decision can have preclusive effect in other cases, even if it would have been reviewed *de novo*." *Id.* at 151–52 (citing Restatement (Second) of Judgments § 28 cmt. a & illus. 1). Finding no "'evident' reason why Congress would not want TTAB decisions to be given preclusive effect," *id.* at 151 (quotations and citation omitted), the

Court held that TTAB decisions are entitled to the preclusive effect that "ordinary preclusion law" requires.

B & B Hardware equally applies to final written decisions of the PTAB. Indeed, the Federal Circuit itself and other courts have repeatedly held that *B & B Hardware* requires courts to give PTAB invalidity determinations preclusive effect. The Federal Circuit, for instance, has recognized that "[t]he TTAB, at issue in *B & B Hardware*, and [PTAB], in this case, are indistinguishable for preclusion purposes." *MaxLinear*, 880 F.3d at 1376; *see also, e.g.*, *Papst Licensing GMBH & Co. KG v. Samsung Elecs. Am., Inc.*, 924 F.3d 1243, 1250–51 (Fed. Cir. 2019) ("Following the Supreme Court's conclusion in *B & B Hardware* that those standards are met by certain adversary proceedings before the Trademark Trial and Appeal Board, we have held that the same is true of an IPR proceeding before the Patent Trial and Appeal Board, so that the issue preclusion doctrine can apply in this court to the Patent Trial and Appeal Board's decision in an IPR once it becomes final." (collecting cases)); *Inland Diamond Prod. Co. v. Cherry Optical Inc.*, __ F. Supp. 3d ___, 2023 WL 6318206, at *4 (E.D. Wis. Sept. 28, 2023) ("The PTAB's decision finding claims 1 and 3 of the '360 and '130 Patents invalid is final and thus estops Plaintiff from relitigating the validity of those claims in this court."

(discussing *B & B Hardware*, 575 U.S. at 148)); *see also infra* § II.B.[3]

4. This Court's rulings in *Commil* and *B & B Hardware*, as well as the foundational principles of preclusion law underlying those decisions, squarely resolve the first question presented. Liquidia did exactly what *Commil* instructed: it secured a final written decision from the PTAB through *inter partes* review that UTC's patent was invalid, and it then sought to use that determination to defeat UTC's claim of induced infringement. Pet. App. 19a. In other words, Liquidia successfully pursued the "proper way[]" to "obtain a ruling" of invalidity, which made Liquidia "immune from liability" for induced infringement. *Commil*, 575 U.S. at 645. Confirming this approach is the Court's holding in *B & B Hardware*—that TTAB determinations are preclusive in infringement litigation, *see* 575 U.S. at 151—which applies equally to TTAB's sister agency, the PTAB. Under this Court's precedent, the Federal Circuit thus should have made quick work of UTC's induced infringement claim. Instead, it broke from this Court's precedent and created uncertainty this Court must now resolve.

---

[3] To the extent that Federal Circuit decisions conflict on this issue—on which it has exclusive appellate jurisdiction—that disagreement itself is reason for this Court's review. *See, e.g.*, *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997) ("The significant disagreement within the Court of Appeals for the Federal Circuit . . . suggests, however, that the doctrine is not free from confusion. We therefore will endeavor to clarify the proper scope of the doctrine.").

II. The Federal Circuit's Decision Conflicts with the Preclusion Principles Applied by This Court and Every Circuit

The Federal Circuit refused to accord preclusive effect to the PTAB's final written decision primarily because it thought that PTAB's decision, while pending on appeal, was a "non-final litigation" without *any* preclusive effect. Pet. App. 20a. The Federal Circuit stands alone among the courts of appeals in this view of preclusion law, which creates unacceptable conflicts with the decisions of this Court and every other circuit.

A. Under Ordinary Preclusion Principles, Agency Decisions Have Preclusive Effect Pending Appeal Absent an Evident Statutory Purpose to the Contrary

As this Court stressed in *B & B Hardware*, "ordinary preclusion law" applies in the context of administrative decisions, absent an "evident" reason that Congress would not want those decisions to receive preclusive effect. 575 U.S. at 151. And as the decisions of this Court and every circuit hold, "ordinary preclusion" law is clear: decisions remain preclusive while on appeal.

1. At a fundamental level, the doctrine of issue preclusion teaches that "the determination of a question directly involved in one action is conclusive as to that question in a second suit." *B & B Hardware*, 575 U.S. at 147 (citation omitted). "Application of [issue preclusion] is central to the purpose for which civil courts have been established, the conclusive resolution of disputes within their jurisdictions." *Montana v. United States*, 440 U.S. 147, 153 (1979).

This Court has reserved the "ultimate authority to determine and declare" the preclusive effect of a federal judgment. *Taylor v. Sturgill*, 553 U.S. 880, 891 (2008).

2. A basic tenet of preclusion law is that a tribunal's decision retains its preclusive effects despite the pendency of an appeal. *See Deposit Bank of Frankfort v. Bd. of Councilmen of City of Frankfort*, 191 U.S. 499 (1903). For example, the Restatement (Second) of Judgments, to which this Court "regularly turns . . . for a statement of the ordinary elements of issue preclusion," *B & B Hardware*, 575 U.S. at 148, explains that "a judgment otherwise final remains so despite the taking of an appeal," Restatement (Second) of Judgments § 13 cmt. f. Likewise, the Wright and Miller treatise explains that "[t]he Supreme Court long ago seemed to establish the rule that a final judgment retains all of its res judicata consequences pending decision of the appeal," and "[t]he lower courts have taken the rule as settled ever since." *Federal Practice and Procedure*, *supra* § 4433 (collecting cases). Moore's, too, provides that "[a]n appeal from a judgment does not automatically suspend operation of the judgment until the determination of the appeal." 20 J. Moore, D. Coquillette, G. Joseph, et al., *Moore's Federal Practice* § 308.10 (3d ed. 2022).

Every single circuit follows this rule as to lower court rulings. *See, e.g.*, *Ross ex rel. Ross v. Board of Educ. of Tp. High School Dist. 211*, 486 F.3d 279, 284 (7th Cir. 2007) (holding that "the fact that an appeal was lodged does not defeat the finality of the judgment" for preclusion purposes); *Commodities Exp. Co. v. U.S. Customs Serv.*, 957 F.2d 223, 228 (6th Cir.

1992) ("[I]t is well established that a final trial court judgment operates as *res judicata* while an appeal is pending."); *Tripati v. Henman*, 857 F.2d 1366, 1367 (9th Cir. 1988) ("The established rule in the federal courts is that a final judgment retains all of its res judicata consequences pending decision of the appeal[.]" (quotations and citation omitted)); *Jaffree v. Wallace*, 837 F.2d 1461, 1467 (11th Cir. 1988) ("The established rule in the federal courts is that a final judgment retains all of its res judicata consequences pending decision of the appeal." (quotations and citation omitted)).[4] The rule is not without its

---

[4] All other circuits are in accord. *See, e.g.*, *In re Belmont Realty Corp.*, 11 F.3d 1092, 1095 (1st Cir. 1993) ("The appeal notwithstanding, the . . . [d]ecision already constituted a final judgment for res judicata purposes."); *Straus v. Am. Pubs.' Ass'n*, 201 F. 306, 310 (2d Cir. 1912) ("The point is also made that the judgment was not res adjudicata because of the appeal pending to the United States Supreme Court. This fact does not suspend the operation of the judgment as an estoppel[.]"); *Cohen v. Superior Oil Corp.*, 90 F.2d 810, 812 (3d Cir. 1937) ("The pendency of an appeal does not prevent . . . a judgment from being res judicata."); *Guinness PLC v. Ward*, 955 F.2d 875, 898 (4th Cir. 1992) (noting "the majority position among the federal courts" that "the existence of a pending appeal does not render a judgment unenforceable nor suspend its preclusive effects absent a party obtaining a stay from either the rendering or enforcing court"); *Stevens v. St. Tammany Par. Gov't*, 17 F.4th 563, 571 (5th Cir. 2021) ("Generally, a judgment is entitled to preclusive effect even though an appeal is pending." (quotations omitted)); *Williams v. Comm'r*, 1 F.3d 502, 504 (7th Cir. 1993) ("What is true is that a judgment final in the trial court may have collateral estoppel effect even though the loser has not exhausted his

drawbacks—it runs the risk of allowing judgments to rest on the preclusive effects of earlier judgments that are subsequently reversed—but courts universally accept those risks, recognizing that "the alternative of retrying the common claims, defenses, or issues is even worse." *Federal Practice & Procedure*, *supra* § 4433.

3. Under this Court's precedent, this rule—that the pendency of an appeal does not disturb a decision's preclusive effect—also applies to agency decisions, such as final written decisions of the PTAB. As this Court explained in *B & B Hardware*, it "regularly turns to the Restatement (Second) of Judgments for a statement of the ordinary elements of issue preclusion," which apply unless "a statutory purpose to the contrary is evident." *B & B Hardware*, 575 U.S. at 148 (citing *Bobby v. Bies*, 556 U.S. 825, 834 (2009); *New Hampshire v. Maine*, 532 U.S. 742, 748–49 (2001); and *Baker v. General Motors Corp.*, 522 U.S. 222, 233, n.5 (1998)). And, as the Restatement explains, "[a]n administrative adjudication becomes

---

appellate remedies."); *In re Ewing*, 852 F.2d 1057, 1060 (8th Cir. 1988) ("It is well established in the federal courts that the pendency of an appeal does not diminish the *res judicata* effect of a judgment rendered by a federal court." (quotations and citation omitted)); *Ruyle v. Cont'l Oil Co.*, 44 F.3d 837, 846 (10th Cir. 1994) ("Under the federal view, the pendency of an appeal does not prevent application of the collateral estoppel doctrine unless the appeal involves a full trial de novo."); *Hunt v. Liberty Lobby, Inc.*, 707 F.2d 1493, 1497 (D.C. Cir. 1983) ("Under well-settled federal law, the pendency of an appeal does not diminish the *res judicata* effect of a judgment rendered by a federal court."); *Pharmacia & Upjohn Co. v. Mylan Pharms., Inc.*, 170 F.3d 1373, 1381 (Fed. Cir. 1999) ("The pendency of an appeal has no effect on the finality or binding effect of a trial court's holding.").

preclusive when it has become final in accordance with the rules stated in §[] 13." Restatement (Second) of Judgments § 83 cmt. a. Section 13 of the Restatement, in turn, provides that "the taking of an appeal" does not alter a judgment's finality. *Id.* § 13 cmt. f. Thus, as *B & B Hardware* recognized, it is hornbook law of issue preclusion that agency decisions like those of the PTAB remain preclusive despite a pending appeal, absent an evident statutory purpose to the contrary.

Numerous courts have confirmed the point, holding that administrative agency determinations have preclusive effect while on appeal. In *Ruyle v. Continental Oil Co.*, 44 F.3d 837 (10th Cir. 1994), for example, the Tenth Circuit held that an order of the Oklahoma Corporation Commission was preclusive in parallel federal litigation, even though the agency's order was on appeal at the time. *Id.* at 845–46 (applying Oklahoma law). As the Tenth Circuit explained, "[u]nder the federal view, the pendency of an appeal does not prevent application of the collateral estoppel doctrine unless the appeal involves a full trial de novo," and the "federal rule is likewise embodied in the *Restatement (Second) of Judgments*," which the Oklahoma Supreme Court in turn follows. *Id.* at 846; *see also Rice v. Dep't of Treasury*, 998 F.2d 997, 999 (Fed. Cir. 1993) (similar). Similarly, in *Chin-Young v. United States*, 774 Fed. App'x 106 (4th Cir. 2019) (unpublished), the Fourth Circuit held that a decision by the Merit Systems Protection Board was preclusive even though it was appealed, explaining that "[f]or administrative preclusion 'it is not necessary that the administrative adjudication have been reviewed and affirmed by a court,'" and "[a]dministrative preclusion means, quite simply, that the MSPB's November 2013

decision on its own achieves preclusive effect." *Id.* at 117 (quoting Restatement (Second) of Judgments § 83 cmt. a.); *see also, e.g.*, *Mahindra & Mahindra Ltd. v. FCA US LLC*, 503 F. Supp. 3d 542, 549–51 (E.D. Mich. 2020) (deeming International Trade Commission decision, then on appeal, preclusive and emphasizing "that trial court judgments are considered final for preclusion purposes even if a party intends to appeal or if an appeal is pending," and though "the present matter involves an administrative agency's decision, [the court] declines to afford less preclusive effect to that decision").

4. The Federal Circuit here split from this precedent in refusing to give the PTAB's decision preclusive effect because it was "on appeal," and thus, in the Federal Circuit's view, a "pending, non-final litigation." Pet. App. 20a. The Federal Circuit cited no authority for that erroneous proposition, other than misconstruing one of its prior decisions to mean that appellate affirmance is *required* for an agency decision to have preclusive effect. *Id.*[5] In effect, the Federal

---

[5] Specifically, the Federal Circuit invoked its prior decision in *XY, LLC v. Trans Ova Genetics, L.C.*, 890 F.3d 1282 (Fed. Cir. 2018), in claiming that "an IPR decision does not have collateral estoppel effect until that decision is affirmed or the parties waive their appeal rights." Pet. App. 20a. That is a misreading of *XY*, which did not hold that an IPR decision lacks preclusive effect once issued. Rather, in that case, the Federal Circuit observed that its affirmance on the same day of the PTAB's determination of invalidity in a parallel IPR "renders final a judgment on the invalidity of the [patent at issue], and has an immediate issue-

Circuit created a carve-out from a basic principle of preclusion law without explaining why.[6]

Notably, even prior to the Federal Circuit's decision in this case, district courts struggled to make sense of the Federal Circuit's preclusion precedent and openly acknowledged their confusion. Some, for example, have stated, as the panel here did, that Federal Circuit law "suggests" that "an IPR decision does not have preclusive effect until that decision is either affirmed or the parties waive their appeal rights"—a result that "seems counterintuitive." *TrustID, Inc. v. Next Caller Inc.*, 2021 WL 3015280, at *3–4 (D. Del. July 6, 2021) (citing *XY*, 890 F.3d at 1294); *see also, e.g.*, *Indivior Inc. v. Alvogen Pine Brook LLC*, 2023 WL 6936749, at *9, *11 (D.N.J. July 10, 2023) (reaching same conclusion and noting "difficulties in harmonizing" Federal Circuit precedent with "traditional" issue preclusion (citing *XY*, 890 F.3d at 1294)). But as explained above, other courts have had little difficulty applying *B & B Hardware* to conclude that PTAB determinations of invalidity *are* indeed preclusive, regardless of any appeals or waiver of appellate rights. *See, e.g.*, *Inland Diamond Prod. Co.*, 2023 WL 6318206, at *4; *supra* p.

---

preclusive effect on any pending or co-pending actions involving the patent." *XY*, 890 F.3d at 1294. Thus, while an appellate affirmance happened to be present in *XY*, the decision did not hold that such an affirmance was *necessary* for a PTAB decision to be preclusive.

[6] The Federal Circuit's reference to whether "the time for appeal has expired or any appeal has terminated" under 35 U.S.C. § 318(b), Pet. App. 20a, likewise refers to the prerequisites for a certificate of cancellation—*not* for a final written decision, which itself has preclusive effect. *See infra* pp. 28–29.

15. These decisions reflect both the errors of the Federal Circuit's reasoning and the confusion it has engendered.

The Federal Circuit's decision now stands in conflict not only with this Court's preclusion precedent, including as set forth in *B & B Hardware*, but also with the decisions of other circuits according preclusive effect to agency decisions (and lower court decisions) more generally while they are pending on appeal. Had this case been decided by another circuit—which it could not have been, given the Federal Circuit's exclusive jurisdiction—basic principles of issue preclusion would have allowed the PTAB's decision to block UTC's induced infringement claim.

Nor can the Federal Circuit's error be cabined to the patent context, or even to that of administrative decisions. Rather, courts routinely look to decisions considering the preclusive effect of agency decisions in deciding how to apply preclusion law to the decisions of other courts, and vice versa. The Federal Circuit's decision thus destabilizes not only preclusion in the patent context, but also more generally the "ordinary preclusion law" that this Court has instructed the lower courts to apply. *B & B Hardware*, 575 U.S. at 151. This Court's intervention is required to restore clarity and stability.

B. The Relevant Statutory Framework Contains No "Evident" Intent to Foreclose Issue Preclusion

As noted, agency decisions have preclusive effect pursuant to ordinary preclusion principles unless "a statutory purpose to the contrary is evident." *B & B*

Hardware, 575 U.S. at 148; *see also id.* at 151 ("[A]bsent a contrary indication, Congress presumptively intends that an agency's determination . . . has preclusive effect."). Further, as this Court has explained, such "administrative estoppel is favored as a matter of general policy," and thus courts apply a "lenient presumption in favor of administrative estoppel." *Astoria Fed. Sav. & Loan Ass'n v. Solimino*, 501 U.S. 104, 109, 112 (1991). The Federal Circuit identified nothing in the relevant statutory scheme that indicates any congressional intent—let alone "evident" intent—to disallow common law preclusion for the PTAB's final written decisions. Nor does any such indicia exist. Ordinary preclusion principles therefore apply in this context.

Certainly, neither the AIA's text nor its structure bars PTAB determinations from having preclusive effect, including while on appeal. To the contrary, Congress enacted statutory estoppel provisions to ensure that issue preclusion would apply fully in the IPR context. Specifically, for parties in civil infringement actions like this one, 35 U.S.C. § 315(e)(2) prevents parties who obtained a final written decision through an IPR from subsequently "assert[ing]" that a patent claim "is invalid on any ground that the petitioner raised or reasonably could have raised during the inter parties review." And for parties before the PTAB, Section 315(e)(1) bars those who have already obtained a final written decision from requesting or maintaining another proceeding before the agency "with respect to that claim on any ground that the petitioner raised or reasonably could have raised during that inter partes review." *Id.* § 315(e)(1).

Hence, the AIA's estoppel provisions ensure that an IPR petitioner—including one who seeks to use an invalidity finding in infringement litigation—must assert *all* grounds for invalidity in the IPR process itself or forever waive those arguments. These provisions demonstrate that Congress envisioned the IPR process as anything but one that is non-final or that may be revisited depending upon developments in subsequent or parallel litigation. Far from evincing any intent to withdraw common law preclusion principles, Congress enacted the AIA to amplify those principles as applied to PTAB's final written decisions. *See, e.g.*, *see also VirnetX, Inc. v. Apple Inc.*, 2014 WL 6979427, at *2 (N.D. Cal. Mar. 21, 2014) ("The plain language of an IPR 'that results in a final written decision' within § 315(e)(2) suggests that estoppel applies once there is a final written decision and not before that time."); *Star Envirotech, Inc. v. Redline Detection*, LLC, 2015 WL 4744394, at *3 n.3 (C.D. Cal. Jan. 29, 2015) ("IPR estoppel attaches once the PTAB issues a final written decision." (citing 35 U.S.C. § 315(b)); *see also* 154 Cong. Rec. S9989 (daily ed. Sept. 27, 2008) (statement of Sen. Kyl) ("This estoppel standard's main purpose appears to be to force a party to bring all of his claims in one forum—everything that he 'could have raised'—and therefore to eliminate the need to press any claims in any other fora.").[7]

---

[7] Addressing the pre-AIA statutory framework, the Federal Circuit has recognized that analogous estoppel provisions for *inter partes* reexamination proceedings "implement[ed] a further codification of common law claim preclusion principles" under *B & B Hardware*. *SynQor, Inc v. Vicor Corp.*, 988 F.3d 1341, 1348 (Fed. Cir. 2021) (discussing 35 U.S.C. §§ 315(c), 317(b) (2006)).

Nor is there any "categorical reason" why the PTAB's final written decisions cannot meet the ordinary elements of issue preclusion. *B & B Hardware*, 575 U.S. at 153 (citing Restatement (Second) of Judgments § 27). The substantive bases for determining that a patent is invalid are identical in IPR proceedings and infringement litigation. *See* 35 U.S.C. § 311(b) (explaining that IPR petitioner may challenge patent claim "only on a ground that could be raised under section 102 or 103").[8] And, as in *B & B Hardware*, there is no "reason to doubt the quality, extensiveness, or fairness" of the PTAB's IPR procedures. *Id.* at 158. Indeed, as this Court has explained, the "patent owner and challenger may seek discovery, file affidavits and other written memoranda, and request an oral hearing." *Return Mail, Inc.*, 139 S. Ct. at 1860 (citing 35 U.S.C. § 316);

---

[8] Invalidity in IPR proceedings must be shown by a preponderance of the evidence, as compared to the clear-and-convincing standard that applies in infringement litigation. These "differing burdens do not defeat issue preclusion," *Fellowes, Inc. v. Acco Brands Corp.*, 2019 WL 1762910, at *6 (N.D. Ill. Apr. 22, 2019), as even the Federal Circuit recognizes, *see XY*, 890 F.3d at 1294 (holding that affirmance of PTAB invalidity finding "has an immediate issue-preclusive effect" in infringement litigation). *Commil* confirms that this difference cannot limit issue preclusion—otherwise, "seek[ing] *inter partes* review at the Patent Trial and Appeal Board and receiv[ing] a decision as to validity" could *never* be used to block an infringement claim, as *Commil* held, even after affirmance. 575 U.S. at 645.

37 C.F.R. pt. 42 (Office Patent Trial Guide, outlining IPR trial procedures).[9]

In its decision here, the Federal Circuit noted that the PTAB's final written decision "does not cancel claims," as claims "are cancelled when the Director issues a certificate confirming unpatentability, which occurs only after 'the time for appeal has expired or any appeal has been terminated.'" 74 F.4th at 1372 (quoting 35 U.S.C. § 318(b)). This has no bearing, however, on whether the PTAB's decision has preclusive effect once issued. Indeed, courts have consistently held that "cancellation" of a patent under Section 318(b) is a "nondiscretionary formality" that does not affect the binding effects of the decision itself. *Sec. People, Inc. v. Iancu*, 971 F.3d 1355, 1361 (Fed. Cir. 2020) (citing 35 U.S.C. § 318(b)). For purposes of obtaining judicial review, for instance, "the certificate of cancellation is irrelevant to the finality of the agency's action, as no agency decision-making is involved in deciding to issue the certificate." *Id.* Nor did this Court in *Commil* hold, or even suggest, that *cancellation* of a patent was required to preclude a finding of infringement. To the contrary, under *Commil*, a party need only seek *inter partes* review

[9] As the Court has stated, in explaining that IPR proceedings have roots in our legal tradition, "history does not establish that patent validity is a matter that, from its nature, must be decided by a court." *Oil States Energy Servs., LLC v. Greene's Energy Grp., LLC*, 138 S. Ct. 1365, 1376 (2018). Indeed, in addition to proceedings between private parties, "there was another means of canceling a patent in 18th-century England, which more closely resembles inter partes review: a petition to the Privy Council to vacate a patent." *Id.* at 1377 (summarizing this history).

and "receive a decision as to validity within 12 to 18 months." *Commil*, 575 U.S. at 645 (citing 35 U.S.C. § 316). The timeframe *Commil* identified pertains only to obtaining a final written decision from the PTAB, not for cancellation—for which the statute prescribes no specific timeline at all—let alone for an appeal to be resolved. *See* 35 U.S.C. § 316(a)(11). In short, under the AIA, the ministerial act of cancellation is simply not a prerequisite to preclusion, and the Federal Circuit was wrong to suggest otherwise.

And beyond the text of the AIA itself, which reveals no intent to displace common law preclusion, the history of the AIA underscores that Congress created the IPR process to prevent duplicative litigation—exactly what the doctrine of issue preclusion accomplishes. "The America Invents Act was designed—after a decade of hearings and revisions—to reduce the cost of patent litigation, to resolve major validity issues in an expert tribunal, and to put an end to repetitive challenges." *SAS Inst., Inc. v. ComplementSoft, LLC.*, 825 F.3d 1341, 1357 (Fed. Cir. 2016) (Newman, J., concurring in part and dissenting in part) (discussing estoppel), *rev'd and remanded sub nom. SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348 (2018). Thus, "[i]n providing a meaningful alternative to district court litigation of these primary issues of patent validity, Congress designed the AIA to achieve expeditious and economical final resolution." *Id.* at 1354; *see also, e.g.*, H.R. Rep. No. 112-98, at 40 (2011) ("The legislation is designed to establish a more efficient and streamlined patent system that will improve patent quality and limit unnecessary and counterproductive litigation costs."); 157 Cong. Rec.

S1363 (daily ed. Mar. 8, 2011) (statement of Sen. Schumer) ("Litigation over invalid patents places a substantial burden on U.S. courts and the U.S. economy.").

Indeed, the statute's record leaves no doubt that Congress sought to ensure that the IPR process would further *enable* the use of preclusion—and thus reduce costly and wasteful infringement litigation. *See, e.g.*, 157 Cong. Rec. S1376 (daily ed. Mar. 8, 2011) (statement of Sen. Kyl) ("Ideally, extending could-have-raised estoppel to privies will help ensure that if an inter partes review is instituted while litigation is pending, that review will completely substitute for at least the patents-and-printed publications portion of the civil litigation."); 157 Cong. Rec. S5409 (daily ed. Sept. 8, 2011) (statement of Sen. Schumer) (stating that the AIA "streamlines review of patents to ensure that the poor-quality patents can be weeded out through administrative review rather than costly litigation"); 157 Cong. Rec. S1362 (daily ed. Mar. 8, 2011) (statement of Sen. Leahy) ("The America Invents Act … will provide more certainty in litigation").

Simply put, the AIA contains no "evident" congressional intent to foreclose the ordinary operation of preclusion law, which here plainly bars UTC's claim of induced infringement. To the contrary, the IPR process as established by Congress aligns perfectly with the general purpose of issue preclusion doctrine, which is to "lay[] legal disputes at rest." *Herrera v. Wyoming*, 139 S. Ct. 1686, 1709 n.6 (2019) (Alito, J., dissenting). The Federal Circuit thus fundamentally misapprehended this statutory scheme, and—particularly given its exclusive

jurisdiction over patent appeals—its flawed decision warrants this Court's review.

III. The Issues Presented Are Exceptionally Important, and This Case Presents an Appropriate Vehicle for Resolution

As explained, the Federal Circuit doubly erred in this case—contrary to this Court's precedent and that of other circuits—in holding that the filing of an appeal strips the PTAB's final written decisions of their preclusive effect. This ruling is not only erroneous, but dangerous, as it threatens to destabilize patent litigation and preclusion law more generally. The rule that a decision—whether of a lower court or an agency—remains preclusive pending appeal is so widely accepted for good reason: it prevents the inefficiency and gamesmanship that would otherwise result. Were preclusion not to apply, a party could ignore an adverse decision and make precisely the claim or argument that had been rejected, so long as it lodged an appeal (whatever its merits) of the decision that did not go its way.

The Federal Circuit's rule, if allowed to stand, would have profound effects on the patent system itself. From 2012 to 2021, 12,607 IPR petitions were filed with PTAB—an average of roughly 1,200 petitions per year. Ken Korea, *Navigating a Decade of the America Invents Act*, ManagingIP (Mar. 1, 2022), https://www.managingip.com/article/2a5d0ugt52wrjolybgu80/navigating-a-decade-of-the-america-invents-act; *see also PTAB Trial Statistics FY22 End of Year Outcome Roundup, IPR, PGR*, United States Patent and Trademark Office 3, https://www.uspto.gov/sites/default/files/documents/p

tab__aia_fy2022_roundup.pdf (noting that PTAB received 1,320 IPR petitions between October 1, 2021 and September 30, 2022). And from 2019 to 2022, the PTAB determined that the claims at issue in its final written decisions were unpatentable or invalid *70% or more* of the time. Industry experts expect these high levels of unpatentability findings to continue into the future. *See What to Expect from the PTAB in 2023: Unpatentability Rates*, Crowell (Jan. 25, 2023), https://www.crowell.com/en/insights/client-alerts/what-to-expect-from-the-ptab-in-2023-unpatentability-rates.

Thus, as a practical matter, the Federal Circuit's decision in this case means that hundreds of invalidity determinations by the PTAB each year will be denied the preclusive effects Congress intended to give them. And infringement cases involving invalid patents will continue to crowd federal court dockets with needless re-litigation of issues the PTAB has already resolved. This is so because, under the Federal Circuit's approach, all that a party who loses in an IPR proceeding needs to do in order to avoid that ruling from taking effect is to file an appeal and pursue an infringement action. Such multiplication of litigation is the opposite of what Congress intended in the AIA.

Moreover, the Federal Circuit's departure from the application of ordinary principles of preclusion in this case cannot be cabined to the PTAB or even to agencies. Preclusion law creates one corpus of principles that courts and agencies alike apply; indeed, courts routinely look to decisions regarding the preclusive effect of *agency* decisions, like the PTAB's here, in determining whether another *court*'s decision is preclusive. *See, e.g.*, *Gen. Star Nat. Ins. Co.*

v. Administratia Asigurarilor de Stat, 289 F.3d 434, 440 (6th Cir. 2002) (evaluating preclusive effect of court decision pending appeal, on the basis of decision considering preclusive effect of agency decision); *Tripati*, 857 F.2d at 1367 (same); *C.F. Tr., Inc. v. First Flight Ltd. P'ship*, 140 F. Supp. 2d 628, 641 (E.D. Va. 2001) (same), *aff'd*, 338 F.3d 316 (4th Cir. 2003). The Federal Circuit's decision here thus creates a ready mechanism not only for agency decisions to be ignored, but for one court to ignore the decision of another court, simply because that decision has been appealed.

The questions presented by this petition will not benefit from further percolation in the circuits. The twelve regional circuits hear patent cases only in extremely rare circumstances. And the Federal Circuit's holding in this case was clear: in language that is certain to be recited in other cases, and that already has been seized upon by commentators,[10] a decision of one tribunal "does not have collateral estoppel effect until that decision is affirmed." Pet. App. 20a.

---

[10] *See, e.g.*, R. Muñoz, J. Weil & K. May, *Lessons in Navigating Collateral Estoppel of Similar Patents*, Law360 (Jan. 8, 2024, 8:25 a.m.), https://www.law360.com/articles/1779586/lessons-in-navigating-collateral-estoppel-of-similar-patents (citing this case and stating that "as opposed to a district court judgment, which may have an immediate preclusive effect, even while an appeal is pending, the [PTAB]'s prior decisions do not have a preclusive effect until they are affirmed on appeal or the time to appeal has passed" (footnote omitted)); Klarquist Sparkman, LLP, *Issue Preclusion*, https://klarquist.com/patent-defenses/issue-preclusion/ (last visited Jan. 19, 2024) (citing this case and stating "a different rule applie[s] to PTAB judgments").

Here, the Federal Circuit not only issued a firm, erroneous decision, but it then refused to correct it on Liquidia's petition for rehearing or rehearing en banc. *See* Pet. App. 92a–93a. The questions presented are thus not only important but ripe for this Court's review.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted,

SANYA SUKDUANG
COOLEY LLP
1299 Pennsylvania Ave.
Suite 700
Washington, DC 20004
(202) 842-7800
ssukduang@cooley.com

KATHLEEN R. HARTNETT
Counsel of Record
COOLEY LLP
3 Embarcadero Center,
20th Floor
San Francisco, CA 94111
(415) 693-2000
khartnett@cooley.com

PATRICK J. HAYDEN
COOLEY LLP
55 Hudson Yards
New York, NY 10001
(212) 479-6000
phayden@cooley.com

ADAM S. GERSHENSON
ALEX ROBLEDO
COOLEY LLP
500 Boylston Street
Boston, MA 02116
(617) 937-2300
agershenson@cooley.com
arobledo@cooley.com

APPENDIX

APPENDIX TABLE OF CONTENTS

APPENDIX A

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2022-2217, 2023-1021

UNITED THERAPEUTICS CORPORATION,

Plaintiff-Cross-Appellant

v.

LIQUIDIA TECHNOLOGIES, INC.,

Defendant-Appellant

Appeals from the United States District Court for the District of Delaware in No. 1:20-cv-00755-RGA-JLH, Judge Richard G. Andrews.

Decided: July 24, 2023

SANYA SUKDUANG, Cooley LLP, Washington, DC, argued for defendant-appellant. Also represented by JONATHAN DAVIES; DEEPA KANNAPPAN, Palo Alto, CA; ERIK BENTON MILCH, Reston, VA.

WILLIAM M. JAY, Goodwin Procter LLP, Washington, DC, argued for plaintiff-cross-appellant. Also represented by WILLIAM COVINGTON JACKSON, JAIME SANTOS, ROHINIYURIE TASHIMA, JENNY J. ZHANG; GERARD JUSTIN CEDRONE, Boston, MA; ADAM WILLIAM BURROWBRIDGE. McDermott Will & Emery, LLP, Washington, DC; DOUGLAS H. CARSTEN, ARTHUR PAUL DYKHUIS, Irvine,

CA; SHAUN R. SNADER, United Therapeutics Corporation, Washington, DC.

Before LOURIE, DYK, and STOLL, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Liquidia Technologies, Inc. ("Liquidia") appeals from a decision of the United States District Court for the District of Delaware holding that (1) claims 1, 4, and 6–8 of U.S. Patent 10,716,793 ("the '793 patent") are not invalid and are infringed by Liquidia and (2) claims 1–3 of U.S. Patent 9,593,066 ("the '066 patent") are invalid as anticipated, but are otherwise infringed by Liquidia. United Therapeutics Corporation ("United Therapeutics") cross-appeals from the court's decision holding that (1) claims 1–3, 6, and 9 of the '066 patent are invalid as anticipated and (2) claims 6, 8, and 9 of the '066 patent are not infringed by Liquidia. *See United Therapeutics Corp. v. Liquidia Techs., Inc.*, 624 F. Supp. 3d 436 (D. Del. 2022) ("*Decision*"). For the reasons provided below, we affirm.

BACKGROUND

United Therapeutics holds New Drug Application ("NDA") No. 022387 for Tyvaso®, an inhaled solution formulation of treprostinil approved for the treatment of pulmonary hypertension ("PH"). Pulmonary hypertension is a potentially life-threatening condition characterized generally by abnormally high blood pressure in the lungs. For many patients, treprostinil is used in treating pulmonary hypertension because it is a vasodilator that reduces vasoconstriction in the pulmonary vasculature, thereby decreasing blood pressure.

Experts consider that there are five subgroups of pulmonary hypertension: Group 1, pulmonary arterial

hypertension ("PAH"); Group 2, pulmonary venous hypertension, *i.e.*, pulmonary hypertension related to left-heart disease; Group 3, pulmonary hypertension associated with disorders damaging the lungs; Group 4, pulmonary hypertension caused by chronic thrombotic or embolic disease, including chronic blood clots in the lungs; and Group 5, a miscellaneous category for conditions that do not fit well into the other four subgroups. Groups 1, 3, 4, and 5 are caused by conditions affecting the pulmonary arteries or precapillary vessels of the lungs ("precapillary PH"), while Group 2 typically develops as a result of a cardiac-based etiology ("postcapillary PH"). Due to differing etiologies, each group may require group-specific treatment.

United Therapeutics owns the '793 and '066 patents, which are generally directed to methods of treating pulmonary hypertension and to pharmaceutical compositions comprising treprostinil. The '793 and '066 patents are listed in the FDA's Orange Book for Tyvaso.

Liquidia filed NDA No. 213005 for Yutrepia™ under § 505(b)(2) of the Food, Drug, and Cosmetic Act (codified at 21 U.S.C. § 355(b)(2)).[1] Yutrepia is a dry powder

[1] Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman amendments to the Food, Drug, and Cosmetic Act), an NDA filed under § 505(b)(2) contains full reports of investigations of safety and effectiveness, where at least some of the information used for approval comes from studies that were not conducted for or by the applicant. Such an NDA is one of two abbreviated approval pathways introduced by the Hatch-Waxman amendments, the other being an abbreviated new drug application ("ANDA") filed under § 505(j) (codified at 21 U.S.C. § 355(j)). 35 U.S.C. § 271(e)(2), the statutory provision delineating acts of infringement, covers both types of applications: "It shall be an act of infringement to submit . . . an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or

inhalation formulation of treprostinil but is not a generic version of any currently marketed drug. Pursuant to § 505(c)(3)(C) (codified at 21 U.S.C. § 355(c)(3)(C)), United Therapeutics sued Liquidia within 45 days of receipt of notice of Liquidia's NDA in the United States District Court for the District of Delaware alleging infringement of the '066 patent. J.A. 171, 190. In addition, after Liquidia filed its NDA, United Therapeutics filed another patent application that eventually issued as the '793 patent, which was subsequently added to the district court litigation. J.A. 208.

In parallel, Liquidia filed a petition for *inter partes* review ("IPR") of the '793 patent, alleging that all claims would have been unpatentable as obvious over prior art at the time of the invention. On July 19, 2022, the Board issued a Final Written Decision finding all claims of the '793 patent unpatentable as obvious. *Liquidia Techs., Inc. v. United Therapeutics Corp.*, No. IPR2021-00406, 2022 WL 2820717 (P.T.A.B. July 19, 2022). United Therapeutics filed a Request for Rehearing, challenging whether various asserted references qualified as prior art. J.A. 36648. In its Rehearing Decision, the Board found that the references were prior art, again holding the claims of the '793 patent unpatentable as obvious. United Therapeutics filed a Notice of Appeal in that case on April 26, 2023. Liquidia filed a motion for expedited appeal, which has been denied. The appeal is currently pending in this court.

I. The '793 Patent

The '793 patent is directed to a method of treating pulmonary hypertension comprising inhalation of

---

described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent[.]"

treprostinil. Asserted claim 1 of the '793 patent is the only independent claim and reads as follows:

> 1. A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

'793 patent at col. 18 ll. 23–31.

The additional asserted dependent claims include limitations directed to dry powder inhalers (claim 4), powder formulations (claim 6), powder formulations comprising particles less than 5 micrometers in diameter (claim 7), and formulations containing no metacresol (claim 8). *See id.* col. 18 ll. 36–37, 40–45.

In the district court, United Therapeutics argued that, although Liquidia's proposed product had not yet been marketed, when marketed, it (1) would directly infringe claims 1, 4, and 6–8 of the '793 patent and (2) would also induce infringement of those claims. Liquidia responded that the asserted claims were invalid as lacking adequate enablement and written description under 35 U.S.C. § 112.

The district court found that United Therapeutics showed that a single administration of treprostinil, as required by claim 1, improves a patient's hemodynamics, establishing that administration of Liquidia's Yutrepia, comprising treprostinil, at the claimed doses will also improve a patient's hemodynamics. The court concluded

that United Therapeutics thus proved by a preponderance of the evidence that the administration of Yutrepia will directly infringe claims 1, 4, and 6–8 of the '793 patent.

The district court also concluded that Liquidia's argument that it lacked specific intent to induce infringement lacked merit. Liquidia argued that, because the Yutrepia label does not encourage administration of a therapeutically effective single event dose, it does not induce infringement. The court noted that the label does not need to provide hemodynamic data to constitute inducement of infringement; instead, it merely needs to instruct doctors and patients to administer a therapeutically effective single event dose. The court found that the label's instructions will inevitably lead to the administration of a therapeutically effective single event dose. The court thus concluded that United Therapeutics proved by a preponderance of the evidence that Liquidia will induce infringement of claims 1, 4, and 6–8 of the '793 patent.

The district court further found that the asserted claims were not invalid for lack of enablement or written description. First, the court construed "treating pulmonary hypertension" as encompassing all five groups of pulmonary hypertension, noting that the specification of the '793 patent expressly includes all five groups when describing "pulmonary hypertension." Second, the court found that a skilled artisan would not need to engage in undue experimentation to practice the full scope of the claimed treatment of pulmonary hypertension, despite potential safety concerns in treating Group 2 PH patients, and that the claims did not require safety and efficacy. Third, the court found that the claims were not invalid for lack of written description, finding that a skilled artisan

would, based on the specification, understand that treprostinil would effectively vasodilate the pulmonary vasculature, improve hemodynamics, and treat a patient's elevated pulmonary blood pressure. As a result of the court's findings that the claims were not invalid but were infringed, the court stayed approval of Liquidia's NDA for Yutrepia until May 5, 2027, the expiration date of the '793 patent.

II. The '066 Patent

The '066 patent is directed to a pharmaceutical composition comprising treprostinil and a process of preparing a pharmaceutical product comprising treprostinil.

Asserted claim 1 of the '066 patent reads as follows:

> 1. A pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof, said composition prepared by a process comprising providing a starting batch of treprostinil having one or more impurities resulting from prior alkylation and hydrolysis steps, forming a salt of treprostinil by combining the starting batch and a base, isolating the treprostinil salt, and preparing a pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof from the isolated treprostinil salt, whereby a level of one or more impurities found in the starting batch of the treprostinil is lower in the pharmaceutical composition, and wherein said alkylation is alkylation of benzindene triol.

'066 patent at col. 17 ll. 51–63.

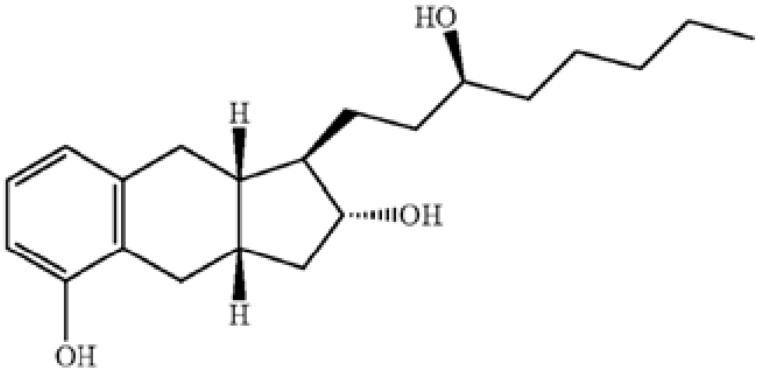
Asserted claim 6 of the '066 patent reads:

> 6. The pharmaceutical composition of claim 1, wherein the isolated salt is stored at ambient temperature.

Id. col. 18 ll. 34–35.

Asserted claim 8 of the '066 patent reads:

> 8. A process of preparing a pharmaceutical product comprising treprostinil or a pharmaceutically acceptable salt thereof, comprising alkylating a triol intermediate of the formula:



> hydrolyzing the resulting compound to form treprostinil, forming a salt of treprostinil stable at ambient temperature, storing the treprostinil salt at ambient temperature, and preparing a pharmaceutical product from the treprostinil salt after storage, wherein the pharmaceutical product comprises treprostinil or a pharmaceutically acceptable salt thereof.

Id. col. 18 ll. 38–61.

Additional asserted dependent claims are directed to crystalline forms (claim 2), a base selected from the group consisting of sodium, ammonia, potassium, calcium,

ethanolamine, diethanolamine, N-methylglucamine, and choline (claim 3), and a pharmaceutical product prepared by the process recited in claim 8 (claim 9). *See id.* col. 17 ll. 64–67; col. 18 ll. 27–28, 62–63.

In the district court, United Therapeutics argued that Liquidia infringed claims 1–3, 6, 8, and 9 of the '066 patent. Liquidia responded that claims 1–3, 6, and 9 were invalid as anticipated by Moriarty[2] and that claims 1–3 and 6 were invalid as lacking written description support. Liquidia did not challenge the validity of claim 8, which is a chemical process claim, in contrast to the other claims that are directed to compositions.

The district court found that United Therapeutics showed by a preponderance of the evidence that Liquidia's Yutrepia would infringe claims 1–3 of the '066 patent because Yutrepia met the impurities limitations of claim 1. But the court also found that claims 1–3, 6, and 9 were invalid as anticipated by Moriarty. Moriarty discloses the synthesis of analogues of benzindene prostacyclins, including treprostinil, which is designated in the publication as UT-15. Moriarty at 1890, 1892. The court also found that Liquidia showed by clear and convincing evidence that the claimed treprostinil product is functionally and structurally the same as the UT-15 treprostinil disclosed in Moriarty. The court thus concluded that claims 1–3 would have been infringed by Liquidia, but for the finding of anticipation, and that claims 6 and 9 were invalid as anticipated by Moriarty but not infringed by Liquidia.

---

[2] R.M. 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. ORGANIC CHEM. 1890 (2004).

In finding a lack of infringement of claim 6, the court construed the terms "ambient temperature" as room temperature (equal to or less than the range of 15°C to 30°C) and "stored"/"storing"/"storage" to have its plain and ordinary meaning. Using these constructions, the court determined that United Therapeutics failed to show by a preponderance of the evidence that Liquidia's Yutrepia production process stored treprostinil at ambient temperature, and therefore found that claims 6, 8, and 9 were not infringed. The court further found that any storage between steps of Liquidia's manufacturing process did not meet the limitations of claims 8 and 9, which require storage of treprostinil before preparing a pharmaceutical product.

The district court also found that the specification provided adequate written description support for the impurities limitation in claim 1, and that a skilled artisan would understand that the inventors were in possession of the composition with the claimed impurities. The court thus concluded that Liquidia did not prove by clear and convincing evidence that claims 1–3 and 6 of the '066 patent were invalid for lack of written description.

In summary, the district court concluded that (1) claims 1, 4, and 6–8 of the '793 patent were not invalid and were infringed by Liquidia; (2) claims 1–3 of the '066 patent were invalid as anticipated by Moriarty and would have been infringed by Liquidia but for the finding of anticipation; (3) claims 6 and 9 of the '066 patent were invalid as anticipated by Moriarty and not infringed by Liquidia; and (4) claim 8 of the '066 patent was not invalid and not infringed by Liquidia. Liquidia appealed, and United Therapeutics cross-appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

Liquidia raises five issues on appeal. First, Liquidia contends that the district court erred in construing the claim limitation "treating pulmonary hypertension" in claim 1 of the '793 patent not to include safety and efficacy. Second, Liquidia argues that the court erred in finding the asserted claims of the '793 patent enabled. Third, Liquidia contends that the court clearly erred in finding the asserted claims of the '793 patent supported by written description. Fourth, Liquidia contends that the court clearly erred in finding Liquidia liable for induced infringement of claims 1, 4, and 6–8 of the '793 patent. Fifth, Liquidia argues that the court clearly erred in finding claims 1–3 of the '066 patent to be infringed.

United Therapeutics raises two issues on cross-appeal. First, United Therapeutics asserts that the district court clearly erred in finding that Liquidia does not infringe claims 6 and 8 of the '066 patent. Second, United Therapeutics contends that the court clearly erred in finding that claims 1–3, 6, and 9 of the '066 patent are invalid as anticipated by Moriarty. We address each appeal and cross-appeal argument in turn.

Infringement is a question of fact that we review, after a bench trial, for clear error. *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1364 (Fed. Cir. 2017). A patent is directly infringed when a person "without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent." 35 U.S.C. § 271(a). "Whoever actively induces infringement of a patent shall be liable as an infringer." *Id*. § 271(b).

We review district court findings of anticipation under 35 U.S.C. § 102 and satisfaction of the written description requirement under 35 U.S.C. § 112 for clear error. *Nuvo Pharms. (Ir.) Designated Activity Co. v. Dr. Reddy's Lab'ys Inc.*, 923 F.3d 1368, 1376 (Fed. Cir. 2019) (written description); *Forest Lab'ys, Inc. v. Ivax Pharms., Inc.*, 501 F.3d 1263, 1268 (Fed. Cir. 2007) (anticipation). Enablement "is a question of law" that we review *de novo* after a bench trial. *Auto. Techs. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1281 (Fed. Cir. 2007). We review questions of claim construction *de novo* but review any underlying facts for clear error. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979, 991 (Fed. Cir. 1995); *Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d 1320, 1328 (Fed. Cir. 2019).

I. The '793 Patent

A.

We first consider Liquidia's challenge to the district court's determination that the meaning of "treating pulmonary hypertension" does not require a showing of safety and efficacy. It asserts that a skilled artisan would understand the plain and ordinary meaning of "treating pulmonary hypertension" to encompass a method that accomplishes that goal safely and effectively. It asserts that the parties' experts agreed that treatment with treprostinil, a vascular dilator, would not benefit Group 2 PH patients. It further asserts that while the specification of the '793 patent states that the treatment does not result in significant side effects, '793 patent at col. 5 ll. 16–20, and that administration of treprostinil is safe, *id.* col. 9 ll. 30– 31, its expert testified that a skilled artisan would have concerns about administering inhaled treprostinil to Group 2 PH patients and that at least one earlier study, in

which a treprostinil-like prostacyclin was administered to Group 2 PH patients, failed due to increased mortality.

United Therapeutics responds that the district court did not err in finding that the claimed administration of treprostinil would improve hemodynamics and hence treat a patient's elevated pulmonary blood pressure, including Group 2 PH patients. It asserts that Liquidia attempts to import limitations into the claims and that nothing in the specification requires the importation of safety and efficacy limitations into the claims. Finally, United Therapeutics asserts that while Liquidia's statements that a skilled artisan would have safety concerns in treating Group 2 PH patients with treprostinil may factor into Food and Drug Administration ("FDA") approval, they do not factor into claim interpretation.

As a threshold matter, we agree with the district court that "treating pulmonary hypertension" includes treating all five groups of pulmonary hypertension patients. The court did not err in finding that the specification encompasses all five groups when describing "pulmonary hypertension." In fact, the specification does not limit the scope of "pulmonary hypertension" to any particular subset of pulmonary hypertension patients. It refers to both "precapillary pulmonary hypertension" and "pulmonary hypertension," which, as the court found, demonstrates that the inventors view precapillary PH only as a subset of the broadly claimed "pulmonary hypertension." Thus, "treating pulmonary hypertension" includes treating all five groups of pulmonary hypertension. *See* '793 patent at col. 9 ll. 36–37, col. 12 ll. 64–65, col. 16 ll. 64–65.

While the claims require "treating pulmonary hypertension comprising administering . . . a therapeutically effective single event dose of a formulation comprising treprostinil," *Decision*, at 467, the district court gave

the phrase "therapeutically effective" a limiting construction. The district court held, and Liquidia does not challenge on appeal, that a person of ordinary skill in the art "would understand the plain and ordinary meaning of 'therapeutically effective single dose' to be a dose given in a single treatment session that causes an improvement in a patient's hemodynamics (reduced PAP or PVR)." *Id.* at 461; Appellee's Br. 39. We need not address whether the district court's construction was correct because Liquidia, on appeal, does not challenge that construction. Read in context, the claim language "treating pulmonary hypertension" does not import any additional efficacy limitations or any safety limitations.

Absent incorporation of safety and efficacy requirements in the claims, Liquidia's argument concerning the safety and efficacy of treating Group 2 PH patients is not before us. Questions of safety and efficacy in patent law have long fallen under the purview of the FDA. *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995) (noting that "the requirements under the law for obtaining a patent" are different from "the requirements for obtaining government approval to market a particular drug for human consumption"); *Scott v. Finney*, 34 F.3d 1058, 1063 (Fed. Cir. 1994) ("Testing for the full safety and effectiveness . . . is more properly left to the [FDA]. Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings."); *In re Anthony*, 414 F.2d 1383, 1395 (CCPA 1969) ("Congress has given the responsibility to the FDA, not to the Patent Office, to determine in the first instance whether drugs are sufficiently safe for use that they can be introduced in the commercial market . . . ."). We decline to insert the FDA's responsibilities into claims by importing requirements where they do not recite such limitations.

B.

We next turn to Liquidia's challenge to the district court's finding that the claims of the '793 patent are adequately enabled and supported by written description. Liquidia argues that the specification of the '793 patent provides no guidance or examples of treating Group 2 PH patients, and thus that a skilled artisan would have to engage in undue experimentation to practice the full scope of the claimed invention (*i.e.*, treating Group 2 PH patients).

Liquidia further argues that, even if the district court's construction of "treating pulmonary hypertension" as not requiring safety was proper, the claims of the '793 patent would still not be enabled because any changes in hemodynamics caused by inhalation of treprostinil would provide no benefit to Group 2 PH patients. Thus, a skilled artisan would not conclude that the '793 patent claims are enabled to the full scope of the claimed invention.

United Therapeutics responds that the district court did not err in concluding that Liquidia failed to show a lack of enablement. It contends that Liquidia failed to show by clear and convincing evidence that enablement would require undue experimentation with respect to Group 2 PH.

Further, even if the specification fails to describe how to treat Group 2 PH patients with treprostinil, United Therapeutics asserts, claims are not required to carve out all possible inoperative embodiments in a claim in order to avoid that claim being found not to be enabled. United Therapeutics asserts that if a skilled artisan has the information to limit the claims to operative embodiments, then the claims are not invalid.

Here, United Therapeutics asserts, the skilled artisan has that information.

Liquidia also challenges the district court's finding that the claims are supported by an adequate written description. Liquidia argues that the '793 patent never describes treating Group 2 PH patients with inhaled treprostinil, but only Group 1, 3, and 4 patients, all of whom have precapillary PH. Thus, Liquidia contends, there is no information in the '793 patent specification sufficient for a skilled artisan to conclude that the inventors were in possession of a method of treating Group 2 PH patients with inhaled treprostinil.

Liquidia further argues that, even if the district court correctly construed "treating pulmonary hypertension" not to require a showing of safety, the claims still are not supported by written description because vasodilation of the pulmonary vasculature is not effective in treating Group 2 PH patients. Thus, Liquidia contends, a skilled artisan would have understood that the inventors did not invent or possess a method of treating Group 2 PH patients.

United Therapeutics responds that the district court did not clearly err in finding the claims of the '793 patent supported by an adequate written description. United Therapeutics argues that Liquidia's written description arguments fail for largely the same reasons as its enablement arguments. In particular, United Therapeutics asserts that the court did not err in holding that a skilled artisan would understand a therapeutically effective dose to be one that improves a patient's hemodynamics. United Therapeutics further contends that, although a physician may or may not decide to administer treprostinil to a Group 2 PH patient, that decision would be informed by FDA guidance, not the written description in the specification.

We agree with United Therapeutics that the claims are adequately enabled as they were construed by the district court. The specification of the '793 patent sufficiently enables the scope of the claims. *See, e.g.*, '793 patent at col. 7 ll. 7–67 (providing details on administration, concentrations, and dosages of inhaled treprostinil for treating patients with pulmonary hypertension); *id.* col. 9 ll. 5–49 (describing an open label study upon acute safety, tolerability, and hemodynamic effects of inhaled treprostinil delivered over the course of a few seconds). While the court credited expert testimony concluding that a physician may have safety concerns in treating Group 2 PH patients with treprostinil and other vasodilators, *see Decision*, at 466–67, the court also found that the record demonstrates that the claimed administration of treprostinil vasodilates the pulmonary vasculature and reduces pulmonary blood pressure even in Group 2 PH patients, *id.* at 468. The court properly relied on expert testimony and record evidence to conclude that a skilled artisan would understand that the claimed administration of treprostinil would vasodilate the pulmonary vasculature, improve hemodynamics, and in this way for a single dose, treat a patient's elevated pulmonary blood pressure independent of the type (*i.e.*, group) of pulmonary hypertension patient. *Id.* That was all that the claims require under the district court's construction because, again, the parties do not dispute that a "therapeutically effective single event dose" is defined by "an improvement in a patient's hemodynamics (reduced PAP or PVP)." That a study—administering treprostinil-like prostacyclins to Group 2 PH patients failed due to increased mortality, yet showed "improvement in a patient's hemodynamics," may be an issue for the FDA. But our focus is on the claimed invention. And on this

record, with the district court's claim construction, the claims are adequately enabled.

We also agree with United Therapeutics that the district court did not clearly err in finding that the claims of the '793 patent are supported by an adequate written description. Written description requires that the specification reasonably convey to those skilled in the art that the inventor had possession of the claimed invention as of the filing date. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). As the court noted, the '793 patent claims require "treating pulmonary hypertension comprising administering . . . a therapeutically effective single event dose of a formulation containing treprostinil," *Decision*, at 466–67, and the specification describes that. In other words, the specification shows possession for the claimed invention under the district court's construction.

Liquidia essentially asks us to treat Group 2 PH as a claimed species within a larger genus (*i.e.*, all five groups of pulmonary hypertension). But analogizing a subset of patients having a variant of a particular disease to traditional genus and species claims is inapt. It would be incorrect to fractionate a disease or condition that a method of treatment claim is directed to, and to require a separate disclosure in the specification for each individual variant of the condition (here, an individual group of pulmonary hypertension patients) in order to satisfy the enablement and written description provisions of 35 U.S.C. § 112, unless these variants are specified in the claims.

Again, because safety and efficacy are not recited in the claims, we need not deal with Liquidia's arguments. Disease-specific treatment requirements are matters for the FDA and medical practitioners. They are best

suited to make these determinations because practitioners are informed by the findings of the regulatory agency to avoid treatment of patients who will not properly respond. And every claim to a method of treatment of an ailment has refinements. That is, for any given method of treatment claim, there may be a subset of patients who would not benefit from or should not take the claimed treatment. *See* Oral Arg. At 4:28–4:58, https://oralarguments.cafc.uscourts.gov/default.aspx?fl=22-2217_0503202 3.mp3. That does not mean that such claims are not sufficiently enabled or supported by written description. A subset of unresponsive patients is not analogous to unsupported species in a generic claim to chemical compounds.

C.

We next turn to Liquidia's challenge to the district court's finding that Liquidia was liable for induced infringement. Liquidia argues that it cannot be held liable for induced infringement because the '793 patent was found to be unpatentable in an IPR, and an unpatentable or invalid patent cannot be infringed. To support this assertion, Liquidia cites *Commil USA, LLC v. Cisco Systems, Inc.*, 575 U.S. 632, 644 (2015) (stating that if "an act that would have been . . . an inducement to infringe pertains to a patent that is shown to be invalid, there is no patent to be infringed"). Liquidia contends that *Commil* should be read as stating that knowledge of actual unpatentability determined in an IPR precludes having the necessary intent to induce infringement.

United Therapeutics responds that the Board's decision on the '793 patent is not final, and a non-final Board decision does not defeat Liquidia's liability for inducing infringement of the '793 patent. United Therapeutics contends that unpatentability is relevant

to infringement liability only once a final adjudication of unpatentability or invalidity rules that there is no such patent to infringe.

We agree with United Therapeutics that the district court did not clearly err in finding that Liquidia induced infringement of the '793 patent. The court did not clearly err in finding that the label on Yutrepia, Liquidia's product, does not need to provide hemodynamic data to constitute inducement of infringement; it merely needs to instruct doctors and patients to administer a therapeutically effective single event dose, which it does. *Decision*, at 462–63. The court also did not clearly err in concluding that United Therapeutics proved that a single administration of Yutrepia will be therapeutically effective, as required by the claims of the '793 patent and constituting inducement.

Liquidia's reliance on *Commil*, 575 U.S. at 632, requires the '793 patent to have been invalidated, but as United Therapeutics argues, the corresponding IPR proceeding of the '793 patent is pending on appeal in this court. A pending, non-final litigation does not negate an intent to infringe that is otherwise supported by evidence. And we have previously held that an IPR decision does not have collateral estoppel effect until that decision is affirmed or the parties waive their appeal rights. *XY, LLC v. Trans Ova Genetics, L.C.*, 890 F.3d 1282, 1294 (Fed. Cir. 2018) ("[A]n affirmance of an invalidity finding, whether from a district court or the Board, has a collateral estoppel effect on all pending or co-pending actions."). Further, as the court noted, the Board's final written decision does not cancel claims; the claims are cancelled when the Director issues a certificate confirming unpatentability, which occurs only after "the time for appeal has expired or any appeal has terminated." 35 U.S.C. § 318(b). The '793

IPR decision thus has no impact here on a finding of induced infringement.

II. The '066 Patent

A.

We next turn to Liquidia's assertion on appeal that the district court clearly erred in finding that it infringed claims 1–3 of the '066 patent. Liquidia argues that United Therapeutics failed to meet its burden of proving infringement. In particular, Liquidia argues that United Therapeutics identified the starting batch as the treprostinil salt and the pharmaceutical composition as the bulk powder. Liquidia thus contends that a comparison between the impurities in the treprostinil salt and bulk powder would have been required to establish infringement of claims that require a lowering of impurities.

United Therapeutics responds that the district court did not clearly err in finding that Liquidia infringed claims 1–3 of the '066 patent. United Therapeutics contends that the court based its conclusion on well-supported facts in finding that a skilled artisan would understand the relevant impurities to be those generated during the alkylation and hydrolysis steps used to create the starting batch of treprostinil.

We need not evaluate this argument that claims 1–3 of the '066 patent are not infringed, because Liquidia correctly argues that the district court did not clearly err in finding those claims invalid as anticipated by Moriarty. *See* Part II.B. Because unpatentable or invalid claims cannot be infringed, *Commil*, 575 U.S. at 644 ("To say that an invalid patent cannot be infringed . . . is in one sense a simple truth, both as a matter of logic and semantics."), the issue of infringe-

ment of claims 1–3 of the '066 patent has been rendered moot.

B.

Accordingly, we forthwith turn to United Therapeutics' argument on cross-appeal concerning the validity of claims 1–3. United Therapeutics argues that Moriarty does not teach the purification of treprostinil through salt formation and discloses no information on specific alkylation and hydrolysis impurities. United Therapeutics argues that it added the relevant impurities claim language to overcome validity challenges raised during prosecution, and the court failed to recognize the structural features that are imparted by the claimed salt-formation purification. United Therapeutics further contends that Moriarty discloses treprostinil with a purity of 99.7%, which does not establish that the product of Moriarty had the same level of alkylation or hydrolysis impurities of the claimed product.

Liquidia responds that the district court did not err in finding that claims 1–3, 6, and 9 of the '066 patent are anticipated by Moriarty. Liquidia argues that the claimed composition in Moriarty is the same as the claimed composition in the '066 patent, and that United Therapeutics demonstrated no clear error in the court's findings.

We agree with Liquidia that the district court did not clearly err in finding that claims 1–3, 6, and 9 are invalid as anticipated by Moriarty. The claims of the '066 patent are directed to a pharmaceutical composition comprising, *inter alia*, treprostinil, prepared by alkylation and hydrolysis steps. It is thus referred to as a product-by-process claim. But a product-by-process claim is a product claim, even if claimed by a process

by which it can be made. The claims also recite the presence of impurities.

We conclude that the district court did not clearly err in finding that these claims are anticipated by the Moriarty reference, which discloses treprostinil with impurities. The specification of the '066 patent discloses an impurity level of 99.7%–99.9%, '066 patent col. 14, table, whereas Moriarty similarly discloses the synthesis of impure treprostinil, designated in the publication as UT-15, having 99.7% purity, Moriarty at 1890, 1892, 1902. As these claims are product claims, they are anticipated by a disclosure of the same product irrespective of the processes by which they are made. Further, United Therapeutics did not provide any expert or fact witness rebutting Liquidia's expert's opinions or providing testimony identifying any structural or functional differences between the Moriarty treprostinil and the claimed treprostinil. *Decision*, at 456. The court thus did not err in finding that claims 1–3, 6, and 9 of the '066 patent are anticipated by Moriarty.

C.

United Therapeutics also argues on cross-appeal that the district court clearly erred in finding that Liquidia does not infringe claims 6 and 8 of the '066 patent. United Therapeutics contends that claims 6 and 8 require that the treprostinil salt be stored at ambient temperature, and that Liquidia stores treprostinil salt at ambient temperature during production, thus infringing the claims. United Therapeutics contends that Liquidia's promise not to make its product with batches of treprostinil salt that were stored at ambient temperature is insufficient to avoid a finding of infringement.

United Therapeutics also contends that the district court erred in construing the term "storage" in claims 6 and 8 as excluding storage during manufacturing but including storage during shipment of the product. United Therapeutics further contends that Liquidia also infringes claim 8 through ambient storage that occurs after the composition recited in claims 1–6 is prepared and before the drug product of claim 8 is prepared.

Liquidia responds that the district court did not clearly err in finding that it does not infringe claims 6 and 8 of the '066 patent. In particular, Liquidia notes that the court based its findings of non-infringement on several clear findings of fact, including that (1) Liquidia's NDA requires the treprostinil salt to be stored at a temperature of 2–8°C; (2) Liquidia asserted that it would not use treprostinil salt batches that have been stored at ambient temperature; and (3) Liquidia begins preparing a pharmaceutical product during step 1 of its production process. Liquidia further asserts that the NDA storage specifications are regulatory requirements, not mere recommendations or promises.

Liquidia further responds that the district court did not err in its construction of the term "storage." Liquidia asserts that United Therapeutics mischaracterizes Liquidia's production process, and that its production process is a single production process, not two stages separated by a period of ambient storage.

We agree with Liquidia that the district court did not clearly err in finding that it does not infringe claims 6 and 8 of the '066 patent. The court credited Liquidia's representations to the FDA that it would store treprostinil sodium between 2°C and 8°C. The court also found that United Therapeutics provided no evidence showing that Liquidia used ambient-

temperature-stored batches of treprostinil in its manufacturing process in making a pharmaceutical composition as required by claim 6 or claim 8. Without a showing that Liquidia stores treprostinil at ambient temperature, there can be no infringement of the claims.

CONCLUSION

We have considered the parties' remaining arguments but find them unpersuasive. For the foregoing reasons, the decision of the United States District Court for the District of Delaware is affirmed.

AFFIRMED

COSTS

No costs.

APPENDIX B

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

C.A. No. 20-755 (RGA) (JLH)

UNITED THERAPEUTICS CORPORATION,

Plaintiff,

v.

LIQUIDIA TECHNOLOGIES, INC.,

Defendant.

FINAL JUDGMENT

At Wilmington, Delaware, this 9th day of September, 2022:

WHEREAS, Plaintiff United Therapeutics Corporation ("UTC") commenced this action against Defendant Liquidia Technologies, Inc. ("Liquidia") asserting infringement of U.S. Patent Nos. 9,593,066 (the "'066 patent"), 9,604,901 (the "'901 patent"), and 10,716,793 (the "'793 patent") by the products that are the subject of Liquidia's New Drug Application No. 213005 seeking approval by the U.S. Food and Drug Administration ("FDA") for the manufacture, use, and sale of its proposed product LIQ861 (YutrepiaTM);

WHEREAS, on January 3, 2022, the Court granted UTC's stipulation of non-infringement of the '901 patent based on the Court's construction of the claim term "contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil,"

with UTC preserving all rights to appeal the Court's construction of that term (D.I. 278);

WHEREAS, at trial, UTC asserted infringement of claims 1, 2, 3, 6, 8, and 9 of the '066 patent and claims 1, 4, 6, 7, and 8 of the '793 patent against Liquidia, and Liquidia asserted counterclaims of non-infringement and invalidity of those claims;

WHEREAS, the Court held a bench trial in the above-captioned action on March 28 to March 31, 2022; and

WHEREAS, the Court issued a Trial Opinion setting forth its Findings of Facts and Conclusions of Law on August 31, 2022 (D.I. 433);

IT IS HEREBY ORDERED AND ADJUDGED:

1. Judgment is hereby entered in favor of Liquidia and against UTC that claims 1, 2, 3, 6, and 9 of the '066 patent are invalid for the reasons set forth in the Court's Trial Opinion of August 31, 2022 (D.I. 433);

2. Judgment is hereby entered in favor of Liquidia and against UTC that Liquidia's proposed LIQ861 product will not infringe claim 6, 8, and 9 of the '066 patent for the reasons set forth in the Court's Trial Opinion of August 31, 2022 (D.I. 433);

3. Judgment is hereby entered in favor of UTC and against Liquidia that Liquidia's proposed LIQ861 product will induce infringement of claims 1, 4, 6, 7, and 8 of the '793 patent, and that those claims are not invalid, for the reasons set forth in the Court's Trial Opinion of August 31, 2022 (D.I. 433); and

4. Pursuant to 35 U.S.C. § 271(e)(4)(A), it is hereby ordered that the effective date of any final approval by the FDA of Liquidia's New Drug Application No.

213005 shall be a date which is not earlier than the expiration date of the '793 patent.

IT IS FURTHER ORDERED:

5. In the event that any party appeals this Final Judgment, any motion for attorneys' fees and/or costs under Fed. R. Civ. P. 54(d) and/or Local Rules 54.1 and/or 54.3, including any motion that this case is exceptional under 35 U.S.C. § 285, shall be considered timely if filed and served within thirty days after final disposition of any such appeal; and

6. In the event that no party appeals this Final Judgment, any motion for attorneys' fees and/or costs under Fed. R. Civ. P. 54(d) and/or Local Rules 54.1 and/or 54.3, including any motion that this case is exceptional under 35 U.S.C. § 285, shall be considered timely if filed and served within thirty days after the expiration of the time for filing a notice of appeal under Federal Rules of Appellate Procedure 3 and 4; and

7. Except as provided herein, all other claims and counterclaims in this action are withdrawn and dismissed with prejudice.

/s/ Richard G. Andrews
The Honorable Richard G. Andrews
United States District Judge

APPENDIX C

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

Civil Action No. 20-755-RGA

UNITED THERAPEUTICS CORPORATION,

Plaintiff,

v.

LIQUIDIA TECHNOLOGIES, INC.,

Defendant.

TRIAL OPINION

Jack B. Blumenfeld, Michael J. Flynn, Sarah E. Simonetti, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, DE; Huiya Wu, GOODWIN PROCTER LLP, New York, NY; William C. Jackson, Eric Levi, GOODWIN PROCTER LLP, Washington, DC; Douglas H. Carsten, Mandy H. Kim, Arthur Dykhuis, Jiaxiao Zhang, Katherine Pappas, MCDERMOTT WILL & EMERY LLP, Irvine, CA; Ian B. Brooks, Adam W. Burrowbridge, Joshua Revilla, Timothy M. Dunker, MCDERMOTT WILL & EMERY LLP, Washington, DC; Harrison Gunn, GOODWIN PROCTER LLP, Boston, MA,

Attorneys for Plaintiff.

Karen E. Keller, Nathan R. Hoeschen, SHAW KELLER LLP, Wilmington, DE; Sanya Sukduang, Jonathan Davies, Douglas W. Cheek, Adam Pivovar, Brittany Cazakoff, COOLEY LLP, Washington, DC; Erik Mulch,

COOLEY LLP, Reston, VA; Ivor Elrifi, COOLEY LLP, New York, NY; Deepa Kannappan, Lauren Krickl, Kyung Taeck Minn, COOLEY LLP, Palo Alto, CA,

Attorneys for Defendant.

August 31, 2022

ANDREWS, U.S. DISTRICT JUDGE:

United Therapeutics Corporation ("UTC") brought this action against Liquidia Technologies, Inc. for infringement of U.S. Patent Nos. 9,593,066 ("the '066 patent"), 9,604,901 ("the '901 patent"), and 10,716,793 ("the '793 patent") under 35 U.S.C. § 271(e)(2)(A). (D.I. 1, 16). I held a four-day bench trial. (D.I. 402-405).[1] The disputes at trial were related to the infringement and validity of claims 1, 2, 3, 6, 8, and 9 of the '066 patent and claims 1, 4, 6, 7, and 8 of the '793 patent. The '901 patent is no longer at issue.

I have considered the parties' post-trial submissions. (D.I. 406, 407, 408, 409, 411, 412, 413, 414, 415, 416, 423, 424). Having considered the documentary evidence and testimony. I make the following findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a).

I. BACKGROUND

UTC is the holder of New Drug Application ("NDA") No. 022387 for Tyvaso®, an inhaled solution formulation of treprostinil approved for the treatment of pulmonary arterial hypertension and pulmonary hypertension associated with interstitial lung disease. (D.I. 322-1, Ex. 1, ¶¶ 5, 12). The '066 and '793 patents are listed in the FDA's Orange Book for Tyvaso®. (*Id*.,

[1] I cite to the trial transcript as "Tr." The trial transcript is consecutively numbered.

¶ 14). The '066 patent discloses an improved process for preparing treprostinil. (*See* JTX 2). The '793 patent discloses a method of administering treprostinil by inhalation. (*See* JTX 3).

Liquidia submitted NDA No. 213005 under § 505(b)(2) of the Federal Food, Drug, and Cosmetic Act seeking FDA approval for the manufacture, use, and sale of its proposed product LIQ861 (Yutrepia™). (D.I. 322-1, Ex. 1, ¶ 2). LIQ861 is a dry powder formulation of treprostinil sodium. (*Id*., ¶ 16). The FDA tentatively approved LIQ861 for the treatment of pulmonary arterial hypertension. (*Id*., ¶¶ 17-18).

Liquidia's NDA contains Paragraph IV certifications alleging that both the '066 and '793 patents are invalid and/or will not be infringed by the manufacture, use, or sale of its proposed product. (*Id*., ¶ 8). UTC received notice of Liquidia's Paragraph IV certifications and initiated the present lawsuit. (*Id.*, ¶ 9).

II. INFRINGEMENT OF THE '066 PATENT

A. Legal Standard

A patent is directly infringed when a person "without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent." 35 U.S.C. § 271(a). Determining infringement is a two-step analysis. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en Banc), *aff'd*, 517 U.S. 370 (1996). First, the court must construe the asserted claims to ascertain their meaning and scope. *Id.* The trier of fact must then compare the properly construed claims with the accused infringing product. *Id.* This second step is a question of fact. *Bai v. L & L Wings, Inc.*, 160 F.3d 1350, 1353 (Fed. Cir. 1998). The patent owner bears the

burden of proving infringement by a preponderance of the evidence. *SmithKline Diagnostics, Inc. v. Helena Lab'ys Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988).

In a Hatch-Waxman case, the plaintiffs infringement claim is based on the accused infringer's future conduct, rather than past acts of infringement. Under § 271(e)(2), the "infringement inquiry . . . is focused on the product that is likely to be sold following FDA approval." *Abbott Lab'ys v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002). "Because drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the []NDA' s description of the drug, an []NDA specification defining a proposed [] drug in a manner that directly addresses the issue of infringement will control the infringement inquiry." *Id.* For product-by-process claims, the infringement inquiry is focused "on the process of making the product as much as it is on the product itself." *Amgen Inc. v. F. Hoffman-La Roche Ltd*, 580 F.3d 1340, 1370 (Fed. Cir. 2009). Thus, "a product-by-process claim is not infringed by a product made by a process other than the one recited in the claim." *Id.*

B. Asserted Claims of the '066 patent

1. A pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof, said composition prepared by a process comprising providing a starting batch of treprostinil having one or more impurities resulting from prior alkylation and hydrolysis steps, forming a salt of treprostinil by combining the starting batch and a base, isolating the treprostinil salt, and preparing a pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof from the isolated treprostinil salt, whereby a level of one or more impurities found in the starting batch of treprostinil is lower in the

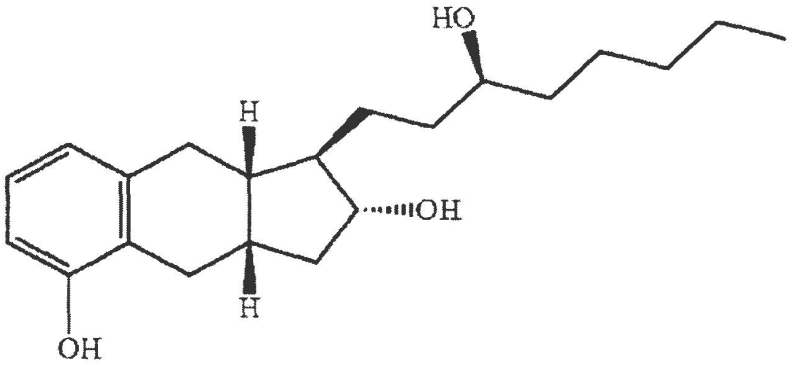
pharmaceutical composition, and wherein said alkylation is alkylation of benzindene triol.

2. The pharmaceutical composition of claim 1, wherein the salt is isolated in crystalline form.

3. The pharmaceutical composition of claim 1, wherein the base is selected from the group consisting of sodium, ammonia, potassium, calcium, ethanolamine, diethanolamine, N-methylglucamine, and choline.

6. The pharmaceutical composition of claim 1, wherein the isolated salt is stored at ambient temperature.

8. A process of preparing a pharmaceutical product comprising treprostinil or a pharmaceutically acceptable salt thereof, comprising alkylating a triol intermediate of the formula:



hydrolyzing the resulting compound to form treprostinil, forming a salt of treprostinil stable at ambient temperature, storing the treprostinil salt at ambient temperature, and preparing a pharmaceutical product from the treprostinil salt after storage, wherein the pharmaceutical product comprises treprostinil or a pharmaceutically acceptable salt thereof.

9. A pharmaceutical product prepared by the process of claim 8.

C. Findings of Fact

1. A POSA would be either a chemical engineer or process research chemist with 3-5 years of experience in API and drug manufacturing or a master's degree in chemistry or chemical engineering who collaborated with individuals having 3-5 years of experience in API drug manufacturing.

2. Yonsung, based in South Korea, manufactures the treprostinil sodium API used to make Liquidia's LIQ861 product. (Tr. at 74:21-75:5 (Nuckolls); PTX 20 at 7). Yonsung has a Drug Master File ("DMF") for the treprostinil sodium used in LIQ861. (PTX 112 (Open DMF); PTX 201 (Restricted DMF)).

3. Yonsung synthesizes the treprostinil sodium by alkylating a batch of benzindene triol ("BTO") to provide a batch of "TN01" (PTX 201 at 7, 22, 35 (DMF Step 10)), then performing a hydrolysis step to provide a batch of treprostinil ("TN02") (*id.* at 8, 23, 36 (DMF Step 11)), and performing a salt formation step by combining the treprostinil with a base (sodium) to yield treprostinil sodium ("TN") (*id.* at 8, 24, 37 (DMF Step 12); Tr. at 75:19-76:20 (Nuckolls); Tr. at 407:2-408:21 (Winkler)).

4. LGM is a U.S. based administrative intermediary between Yonsung and Liquidia. (Tr. at 346:7-10 (Kindig); Tr. at 439:2-5 (Winkler)). Yonsung's shipments of treprostinil sodium sometimes go through LGM to Liquidia; however, LGM does not manufacture treprostinil sodium, nor is it involved in the development or administration of Liquidia's LIQ861 product. (Tr. at 331:14-21 (Kindig); Tr. at 366:5-16 (Lenox)).

5. A POSA would understand that the impurities limitations in claim 1 of the '066 patent refer to any impurities generated during the process steps of alkylating and hydrolyzing a batch of BTO (including from side reactions, impurities in reagents, solvents, or starting materials).

6. Yonsung's analytical testing of treprostinil sodium is a reliable and accurate measure of impurities in the pharmaceutical composition resulting from the alkylation and hydrolysis steps; Liquidia's processing of the TN into the pharmaceutical composition (LIQ861 bulk powder) does not affect those impurities.

7. Liquidia's proposed LIQ861 product will be prepared by a process which lowers the level of one or more impurities resulting from prior alkylation and hydrolysis steps as claimed in the '066 patent. The percentage of total "related substance" impurities and the amount of total "related substance" impurities increase during the alkylation and hydrolysis steps from BTO to the starting batch of treprostinil (TN02), and then decrease in the TN batch after the salt formation and isolation steps.

8. Liquidia's NDA and Yonsung's DMF require treprostinil sodium to be stored at 2°C to 8°C.

9. Liquidia will not use treprostinil sodium batches which have been stored at ambient temperature for GMP manufacturing.

10. Liquidia begins preparing a pharmaceutical product during Step 1 of its PRINT process.

D. Conclusions of Law

1. Claims 1, 2, and 3

Liquidia only disputes infringement of the impurities limitations in claims 1,2, and 3. Claim 1 recites

"providing a starting batch of treprostinil having one or more impurities resulting from prior alkylation and hydrolysis steps . . . wherein said alkylation is alkylation of benzindene triol." As a preliminary issue, the parties dispute the proper construction of "impurities resulting from prior alkylation and hydrolysis steps." Liquidia argues that the claimed impurities must result from alkylation and hydrolysis of "BTO," not the alkylation and hydrolysis of any compound that may be present in the reaction vessel. (D.I. 411 at 3). UTC argues that the claimed impurities encompass any impurities generated during the process steps of alkylating and hydrolyzing a batch of BTO (including from side reactions, impurities in reagents, solvents, or starting materials). (D.I. 408 at 7-8).

UTC's construction is correct. The claim language requires that the impurities result from the "prior alkylation and hydrolysis *steps."* A POSA would understand that the alkylation step involves alkylating all materials in a batch of BTO, not just the single alkylation reaction of BTO. (*See* Tr. at 110:23-111:10 (Nuckolls); Tr. at 810:16-19, 818:18-22 (Scheidt); *see also* Tr. at 423:15-20 (Winkler) ("[A] real batch of – a bottle of benzindene triol could contain impurities.")). Thus, I find that a POSA would understand that any impurities generated during the alkylation and hydrolysis steps (including from side reactions) are within the scope of the claim.

Claim 1 further recites: "whereby a level of one or more impurities found in the starting batch of treprostinil is lower in the pharmaceutical composition." UTC has identified the LIQ861 bulk powder as the "pharmaceutical composition" and Yonsung's TNO2 as the "starting batch of treprostinil." Liquidia argues that UTC cannot prove infringement of this limitation because UTC's

experts only compared the impurities between TNO2 and TN, not the LIQ861 powder. (D.I. 411 at 2). UTC responds that Yonsung's impurities testing for TN is a proper measure of impurities in the pharmaceutical composition resulting from the alkylation and hydrolysis steps because Liquidia's processing of TN into LIQ861 bulk powder has no effect on the impurities from these steps. (D.I. 416 at 4). Once Liquidia receives the TN from Yonsung, Liquidia uses its proprietary PRINT process[2] to prepare the LIQ861 bulk powder using the TN as the API. (DTX 204; PTX 20). In simple terms, Liquidia puts the TN in solution, adds excipients, and dries this formulation into the powder. (DTX 204 at 2-6; Tr. at 741:7-16 (Gonda)).

UTC's expert Dr. Nuckolls testified that he "wouldn't expect" Liquidia's processing of TN to impact the impurities from the alkylation and hydrolysis steps. (Tr. at 157:7-17 (Nuckolls); *see also* PTX 66 at 96 ("Treprostinil sodium drug substance process impurities are controlled by the manufacturer, Yonsung Fine Chemicals Co., Ltd. (Yonsung)."). Dr. Nuckolls also testified that it would be difficult for a POSA to test the impurities resulting from the alkylation and hydrolysis steps in the LIQ861 bulk powder because the composition has been mixed with other excipients. (Tr. at 133:25-134:3 (Nuckolls)). Liquidia has not provided any expert testimony to rebut these opinions; thus, I will credit Dr. Nuckolls' testimony on this point. I therefore find that the TN impurities are representative of the impurities in the "pharmaceutical composition" (LIQ861 bulk powder) resulting from the prior alkylation and hydrolysis steps. *Cf. Vectura Ltd. v. GlaxoSmithKline LLC*, 397 F. Supp. 3d 579,587-88 (D. Del. 2019) (finding

[2] PRINT stands for Particle Replication in Nonwetting Templates. (DTX 204 at 2).

that comparison testing supported the jury's infringement verdict where there was evidence that the tested products were representative of the accused products), *aff'd*, 981 F.3d 1030 (Fed. Cir. 2020).

To prove infringement of the impurities limitations, UTC compared the (1) amount of total impurities; (2) number of total impurities; and (3) amount of *epi*-treprostinil in BTO, TN02, and TN.

First, Dr. Nuckolls analyzed the total "related substance" impurities data provided by Yonsung in its DMF. (*See* PTX 201 at 270-72).[3] For two of the three DMF validation batches (TN117I010, TN117K010), the percentage of total "related substance" impurities increased between BTO and TN02, and then decreased in TN.[4] (Tr. at 77:23-80:18 (Nuckolls); PTX 201 at 270-72; PTX 326 at 4 (identifying the corresponding BTO, TN01, and TN02 batch numbers for each TN batch number)). Dr. Nuckolls opined that these changes in the percentage of total "related substance" impurities between BTO, TN02, and TN show infringement of the impurities limitations. (Tr. at 77:23-80:18 (Nuckolls)).

---

[3] Because Liquidia relies on the same impurities data in its NDA, I find these data to be reliable. (*See* PTX 66 at 96; PTX 105 at 7-11).

[4] For validation batch TN117I010, the percentage of "related substance" impurities was 0.07% in BTO, 0.20% in TN02, and 0.03% in TN. (PTX 201 at 270-72). For validation batch TN117K010, the percentage of "related substance" impurities was 0.08% in BTO, 0.20% in TN02, and 0.01% in TN. (*Id.*). These results are consistent with Yonsung's acceptance criteria, which allow for a greater percentage of "related substance" impurities in TN02 than in TN. (*Id.* (2.0% for TN02; 0.5% for TN)). For validation batch TN117K020, the percentage of "related substance" impurities was 0.3 8% in BTO, 0.21% in TN02, and 0.01% in TN. (*Id.*).

Second, Dr. Nuckolls analyzed the number of total impurities detected in Yonsung's validation batches. To do so, Dr. Nuckolls looked at Yonsung's underlying high-performance liquid chromatography (HPLC) data. (Tr. at 81:8-84:19 (Nuckolls)). HPLC separates components in a mixture by running the mixture down a column. (Tr. at 81:8-23 (Nuckolls)). The mixture's components are separated based on how they interact with the column, so each component will elute at different retention times, depicted by peaks on a chromatogram. (*Id.;* Tr. at 176:3-18 (Toste)).

To determine the number of impurities, Dr. Nuckolls counted the number of HPLC peaks in the chromatograms for BTO, TN02, and TN, excluding the peaks for "the material of interest" (e.g., BTO, TN02, and TN) and for the "known impurities" that were "labeled as missing or not detected." (Tr. at 81:24-83:4 (Nuckolls)). For example, the chromatogram for TN02 for validation batch TN117I010 reported six peaks. (PTX 1540 at 79-80). One of these peaks identified TN02, which is the material of interest, not an impurity. (*Id.*). Thus, this peak was excluded from the impurities count. The chromatogram also identifies "15-epi-Treprostinil" and "Treprostinil ethyl ester" as "Peak Names," but reports these impurities as "Missing." (*Id.*). Because these known impurities were not detected in this sample, they are also excluded from the impurities count. Accordingly, Dr. Nuckolls identified three "related substance" impurities in this batch of TN02. (Tr. at 82:3-83:4 (Nuckolls)). Dr. Nuckolls testified that for two validation batches (TN117I010, TN117K010), the number of "related substance" impurities increased between BTO and TN02, and then decreased in TN.[5]

[5] For validation batch TN117I010, one "related substance" impurity was identified in BTO, three "related substance" impurities were

(Tr. at 81:24-84:19 (Nuckolls)). Dr. Nuckolls testified that this decrease shows that one or more impurities resulting from the alkylation and hydrolysis steps are lowered from TN02 to TN. (*Id.*).

Liquidia argues that Dr. Nuckolls has failed to show a reduction in impurities "resulting from prior alkylation and hydrolysis steps . . . wherein said alkylation is alkylation of benzindene triol." (D.I. 411 at 4). Liquidia argues that the reported "total impurities" relied on by Dr. Nuckolls in his amount of total impurities analysis include "residual solvents and any impurity contained in the reagents or starting materials, not just impurities resulting from the claimed process steps." (*Id.*). Liquidia similarly faults Dr. Nuckolls' number of impurities analysis. Liquidia argues that since Dr. Nuckolls failed to correlate the unidentified HPLC peaks to any specific impurity, he cannot show that these impurities resulted from the alkylation and hydrolysis steps. (*Id.*).

These arguments, however, rely on Liquidia's improper interpretation of the impurities limitations. As concluded above, a POSA would understand that the claimed impurities include any impurities generated during the alkylation and hydrolysis steps, including impurities originating from starting materials or reagents. Thus, Liquidia's arguments rest on an infirm foundation.

---

identified in TN02, and one "related substance" impurity was identified in TN. (Tr. at 82:3-83:4 (Nuckolls); PTX 1536 at 51 (BTO); PTX 1539 at 77 (TN); PTX 1540 at 79-80 (TN02)). For validation batch TN117K010, two "related substance" impurities were identified in BTO, three "related substance" impurities were identified in TN02, and one "related substance" impurity was identified in TN. (PTX 1410 at 59-62 (BTO); PTX 1157 at 33-34 (TN02); PTX 1543 at 83-84 (TN)). The underlying HPLC chromatogram for validation batch TN117K020 was not available to Dr. Nuckolls. (Tr. at 84:14-19 (Nuckolls)).

As described in its DMF, Yonsung uses a twelve-step process to manufacture TN. (PTX 201 at 3). Step 10 of this process is the alkylation step—BTO is reacted with the alkylating agent to produce TN01. (Tr. at 75:20-76:2, 76:11-13 (Nuckolls); PTX 201 at 7). Next, in Step 11—the hydrolysis step—TN01 is hydrolyzed to produce TN02. (Tr. at 76:1-3, 13-15 (Nuckolls); PTX 201 at 8). In Step 12, TN02 is treated with a base to form TN. (Tr. at 76:3-5, 15-18 (Nuckolls); PTX 201 at 8). Thus, Dr. Nuckolls opined that any increased impurities in TN02 as compared to BTO resulted from the alkylation and hydrolysis steps, because those were the steps that were run to synthesize TNO2 from BTO. (Tr. at 80:4-18, 82:3-15 (Nuckolls)). He further opined that the impurities that were generated during the alkylation and hydrolysis steps (Steps 10 and 11) were reduced during the final salt formation step (Step 12), as shown by the reduced levels of impurities in TN as compared to TN02. (*Id.*). I credit Dr. Nuckolls' testimony over Dr. Winkler's contrary testimony, which relied on Liquidia's erroneous construction. (*See* Tr. at 427:19-429:17 (Winkler)).

Based on the total impurities analyses conducted by Dr. Nuckolls, I find that UTC has proven that Liquidia will meet the impurities limitations of claim 1.[6] I therefore find that UTC has proven by a preponderance of the evidence that Liquidia's proposed LIQ861 product will infringe claims 1, 2, and 3 of the '066 patent.[7]

---

[6] Because I find UTC's first two analyses sufficient to show infringement, I need not consider UTC's third analysis, which compares the amount of epi-treprostinil in TN02 and TN.

[7] "To be sure, if at the end of the day, an act that would have been an infringement . . . pertains to a patent that is shown to be invalid, there is no patent to be infringed." *Commil USA, LLC v. Cisco Sys., Inc.,* 575 U.S. 632, 644 (2015). Since I ultimately

2. Claim 6

Claim 6, which depends from claim 1, further requires that "the isolated salt is stored at ambient temperature" before it is used to prepare a pharmaceutical composition. I construed "ambient temperature" as "room temperature (equal to or less than the range of 15°C to 30°C)." (D.I. 119). I construed "stored"/"storing"/"storage" to have its plain and ordinary meaning. (*Id.*).

Liquidia has represented to the FDA that it will store treprostinil sodium between 2°C and 8°C. Yonsung's DMF, which is incorporated in Liquidia's NDA (*see* PTX 105 at 3), specifies the following storage conditions for TN: "STORAGE: Should be kept in a tight container, protected from moisture and light and stored at 2°C to 8°C." (PTX 112 at 517). The certificates of analysis for TN and Yonsung's 2017 List of Finished and Intermediate Products also include these storage requirements. (*Id.* at 448, 450 ("Storage condition: Should be kept in a tight container, protected from moisture and light and stored at 2 °C to 8 °C (Long-term storage)."); DTX 43 at 6 (specifying TN's "Storage Conditions" as "Refrigerated")). LGM, an intermediary between Yonsung and Liquidia, stores TN in accordance with Yonsung's set storage conditions. (Tr. at 365:23-366:4, 367:9-15, 368:2-7 (Lenox); *see also* DTX 105). Liquidia's raw material specification for treprostinil sodium states: "Storage Conditions: 2° - 8°C, protected from light and moisture." (DTX 9 at 1; *see also* Tr. at 374:12-15, 396:7-10 (Fuson) (testifying that the FDA would expect Liquidia to follow the temperature storage conditions set in its raw material specification and Yonsung's DMF); DTX 407 at 3 (FDA pre-approval inspection report wherein

---

conclude that claims 1, 2, and 3 of the '066 patent are invalid as anticipated, there is ultimately no infringement.

the FDA checked Liquidia's compliance with the 2°C to 8°C storage conditions)).

Despite these clear statements to the FDA, UTC argues that Liquidia's NDA and Yonsung's DMF permit storage of TN at ambient temperature because Yonsung's stability data show that TN is stable at ambient temperature. (*See* PTX 112 at 519-61). The parties' FDA experts Mr. Matto and Mr. Fuson both agree that if there were an out-of-specification temperature excursion (e.g., TN was exposed to ambient temperatures), Liquidia would need to conduct a full investigation before using that TN to make LIQ861. (Tr. at 272:9-274:3 (Matto); Tr. at 378:1-15 (Fuson)). But the fact that Liquidia might, in some circumstances, be permitted to use TN exposed to ambient temperatures is insufficient to show that Liquidia will do so.[8] *See Fujitsu Ltd v. Netgear Inc.*, 620 F.3d 1321, 1329 (Fed. Cir. 2010) ("[I]t is not enough to simply show that a product is capable of infringement; the patent owner must show evidence of specific instances of direct infringement.").

---

[8] UTC argues that Liquidia infringes as a matter of law under *Sunovion*. (D.I. 408 at 10-11). *Sunovion* is inapposite. The patent claim at issue in that case limited the concentration of a particular isomer to "less than 0.25%," and the amended ANDA specified a product containing "[not more than] 0.6%" concentration of the same isomer. *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.,* 731 F.3d 1271, 1274-75 (Fed. Cir. 2013). Since the ANDA specification of not more than 0.6% necessarily included products meeting the claim limitation of less than 0.25%, the Court held that Defendant had sought "FDA approval to market a generic compound within the scope of a valid patent," and thus infringed as a matter of law. *Id.* at 1280. In contrast, here, Liquidia asks the FDA to approve sales that fall outside the scope of the '066 patent. Liquidia's NDA (through incorporation of Yonsung's DMF) specifically provides that TN should be stored at 2°C to 8°C, not ambient temperature.

UTC further argues that the isolated salt (TN) used to make LIQ861 is stored at ambient temperature at three points in the process: before acceptance into Yonsung's warehouse; during shipment from Yonsung to Liquidia; and during Step 1 of Liquidia's PRINT process. (D.I. 408 at 10). I will address each argument in turn.

First, UTC asserts that TN is stored at ambient temperature in "finished product storage containers" before acceptance into Yonsung's warehouse. Relying on Yonsung's 2017 batch production record for TN1171010, Dr. Nuckolls claimed that Yonsung stored the TN at ambient temperature for 43 days between production and acceptance into the warehouse. (Tr. at 96:10-97:24 (Nuckolls); PTX 1409 at 47-50, 70). Dr. Nuckolls, however, only based his opinion on the lack of temperature notation in this batch record. The absence of temperature notation on a single batch record does not show storage at ambient temperature by a preponderance of the evidence. Rather, Yonsung's List of Finished/Intermediate Products from 2017 required TN to be stored at refrigerated temperatures. (DTX 43 at 6). Further, batch production records from 2019 indicate that TN is "refrigerated" between production and acceptance into the warehouse. (DTX 413 at 12).

Second, UTC contends that TN is stored at ambient temperature when it is shipped from Yonsung to Liquidia.[9] Three batches of TN (TN1200010, TN120G010,

[9] Liquidia argues that the plain and ordinary meaning of "stored" does not include shipping. (D.I. 412 at 8 n.2). I disagree. A POSA would understand that a material can be stored during shipment. (Tr. at 137:6-138:11 (Nuckolls)).

and TN120I010)[10] experienced ambient temperatures for nine days during shipment from Yonsung to LGM. (PTX 19 at 17, 19-21, 26-27; Tr. at 98:1-13 (Nuckolls)). LGM notified Liquidia that these batches experienced temperature excursions, stating, "[O]ur QC released the shipment because Yonsung has long-term stability showing the Treprostinil is stable at room temperature for 6 months." (PTX 2020 at 475-78). Liquidia accepted these shipments, marking "Requirements Met" for "Transport Conditions (Temperature-if applicable)" on the receiving reports. (PTX 19 at 1; PTX 104 at 1).

UTC provides no evidence showing that Liquidia used these batches in GMP manufacturing to make a pharmaceutical composition, as is required by claim 6. Instead, the evidence shows that Liquidia only used these batches for R&D. Liquidia's Executive Director of Analytical Operation, Mr. Kindig, testified that TN120C010 was ordered specifically for use in R&D, not GMP manufacturing. (Tr. at 309:1-4, 321:1-13 (Kindig)). Mr. Kindig also testified that TN120G010 and TN120I010 were rejected by Liquidia's Quality Unit for GMP use and were relegated to R&D use only. (Tr. at 317:1-320:20 (Kindig)).[11] The fact that Liquidia accepted these out-of-specification batches instead of requesting a refund from Yonsung is not persuasive

[10] These batches are not listed as "Representative Treprostinil Sodium Drug Substances Batches" in the NDA. (PTX 105 at 8).

[11] Nevertheless, UTC again argues that the FDA will permit Liquidia to use these batches because of Yonsung's stability data. (D.I. 408 at 13-14). But, as discussed above, this does not show by a preponderance of the evidence that Liquidia will use batches exposed to ambient temperatures to prepare pharmaceutical compositions. Liquidia rejected these batches for GMP manufacturing because they were exposed to ambient temperatures, and UTC has failed to provide evidence showing that Liquidia will not continue to do so.

evidence of infringement, as Liquidia had another use for these batches.

UTC also asserts that three other batches of TN (TN116J010, TN117K010, and TN117I010) were stored at ambient temperature during shipment and were subsequently used for clinical trials. (*See* PTX 105 at 8 (listing these batches as "Representative Treprostinil Sodium Drug Substances Batches")). While the temperature data loggers for these batches do show a spike to ambient temperature, this spike directly corresponds with Liquidia's receipt of the batches. (PTX 116; PTX 117; Tr. at 324:11-327:24 (Kindig); Tr. at 150:17-153:22 (Nuckolls) (confirming that receipt date and spike date were both December 11, 2017)). Once Liquidia receives the TN shipment, an employee will open the box, set aside the data logger and paperwork, and transfer the TN to the GMP refrigerator. (Tr. at 321:18-323:7 (Kindig)). Because the temperature logger does not automatically stop once the box is opened, the employee will later press the button to stop the data logging when dealing with the paperwork. (Tr. at 322:15-323:2; 327:18-328:8 (Kindig)). This explains why the data loggers immediately spiked into ambient temperature on the date Liquidia received and opened the box. Thus, the temperature data loggers for these three batches do not prove storage at ambient temperature.

The remaining shipments that UTC points to did not include temperature data loggers. (PTX 123; PTX 124; PTX 127; PTX 823; *see also* PTX 126 at 24 (temperature logger showing a maximum temperature of 6.1°C)). Contrary to UTC's assertion, the lack of temperature data is not persuasive evidence that these batches were stored at ambient temperature.

Third, UTC argues that TN is stored at ambient temperature in a drybox during Step 1 of Liquidia's

PRINT process. Liquidia's PRINT process has six steps: (1) "Preparation of aqueous stock solution"; (2) "Preparation of engineered particles (particle fabrication)"; (3) "Dry collection of engineered particles as bulk LIQ861 inhalation powder"; (4) "Drying and packaging of bulk LIQ861 inhalation powder"; (5) "Drug Product Primary Packaging — encapsulation of bulk LIQ861 inhalation powder in [HPMC] capsules"; and (6) "Drug Product Secondary Packaging — blister packaging and assembly of commercial drug product kit." (DTX 204 at 2). After Step 4, the LIQ861 bulk powder is shipped to Xcelience for encapsulation and packaging (Steps 5 and 6). (*Id.* at 12).

During Step 1, a sample of TN is placed in a drybox and used to make a stock aqueous solution. (PTX 70 at 9-17). Dr. Nuckolls claims that TN is "stored" in the drybox for three hours. (Tr. at 99:24-100:7 (Nuckolls) (relying on the time stamps in Step 2-2 (8:12am) and Step 2-17 (11:46am) of the Batch Production Record (PTX 70))). A POSA, however, would understand that TN is being used, not stored, during Step 1 of the PRINT process. (*See* DTX 204 at 2 (referring to the PRINT process as "[t]he manufacturing process"). Thus, evidence that Liquidia places TN in a drybox does not prove infringement of the storage limitation.

Liquidia has represented to the FDA that it will store treprostinil sodium at 2°C to 8°C. UTC has failed to prove that Liquidia will go against these representations and store isolated treprostinil sodium at ambient temperature before it is used to prepare a pharmaceutical composition. *See In re Brimonidine Pat. Litig.*, 643 F.3d 1366,1378 (Fed. Cir. 2011) ("We cannot assume that [the NDA filer] will not act in full compliance with its representations to the FDA."). Accordingly, I find that UTC has failed to prove by a

preponderance of the evidence that Liquidia's proposed LIQ861 product will infringe claim 6.

3. Claims 8 and 9

Liquidia only disputes infringement of the temperature storage limitation in claims 8 and 9. Claims 8 and 9 require "storing the treprostinil salt at ambient temperature, and preparing a pharmaceutical product from the treprostinil salt after storage." UTC asserts that the three instances of storage discussed above with respect to claim 6 apply equally to claims 8 and 9. (D.I. 408 at 16). This evidence fails to show storage of TN at ambient temperature for the reasons discussed above.

Because claims 8 and 9 require storage of "the treprostinil salt," whether isolated or not, UTC points to three additional instances of storage at ambient temperature to show infringement. Specifically, UTC contends that the LIQ861 bulk powder, which contains the treprostinil salt after it is mixed with excipients, is stored at ambient temperature between PRINT Steps 1 and 2; between PRINT Steps 2 and 3; and between PRINT Steps 3 and 4. (*Id.*).

Claim 8 recites a method for "preparing a pharmaceutical product," while claim 6 recites a "pharmaceutical composition." UTC contends that the LIQ861 bulk powder is the "pharmaceutical composition" and LIQ861 is the "pharmaceutical product." (*Id.*). UTC asserts that Liquidia prepares the pharmaceutical composition during PRINT Steps 1-4 and begins "preparing a pharmaceutical product" at PRINT Step 5. (*Id.*). I disagree. I find that a POSA would understand that Liquidia begins preparing the LIQ861 product at

PRINT Step 1, not Step 5.[12] Steps 5 and 6 simply involve encapsulating and packaging the LIQ861 inhalation powder produced in Step 4, i.e., putting it in final dosage form. (Tr. at 455:9-12 (Winkler); DTX 204 at 2). A POSA would understand that the encapsulation and packaging performed during these steps would not change the chemical properties of the bulk LIQ861 inhalation powder produced in Step 4. (Tr. at 455:5-18 (Winkler)). Accordingly, a POSA would understand that Liquidia begins preparing a pharmaceutical product before the final packaging steps.

Any "storage" between steps in the PRINT process thus cannot meet the limitations of claims 8 and 9, which require storage before preparing a pharmaceutical product. I therefore find that UTC has failed to prove infringement of claims 8 and 9 by a preponderance of the evidence.[13]

III. INVALIDITY OF THE '066 PATENT

A. Product-by-Process Claims (Claims 1, 2, 3, 6, and 9)

1. Legal Standard

"In determining validity of a product-by-process claim, the focus is on the product and not on the process of making it." *Amgen Inc. v. F. Hoffman-La*

---

[12] While I agree with UTC that a POSA would understand the "pharmaceutical product" of claim 8 to be distinct from the "pharmaceutical composition" of claim 6, this does not mean that the preparation of the pharmaceutical composition and pharmaceutical product cannot begin at the same point.

[13] Liquidia also argues that UTC has failed to show that Liquidia uses "a salt of treprostinil stable at ambient temperature" as required by claims 8 and 9. (D.I. 411 at 12). Because I have found that UTC has failed to prove infringement of the storage limitation, I need not address this argument.

Roche Ltd, 580 F.3d 1340, 1369 (Fed. Cir. 2009). "That is because of the . . . long-standing rule that an old product is not patentable even if it is made by a new process." *Id.* at 1370. "If the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985). However, there is an exception to this general rule when "the process by which a product is made imparts 'structural and functional differences' distinguishing the claimed product from the prior art." *Greenliant Sys., Inc. v. Xicor LLC*, 692 F.3d 1261, 1268 (Fed. Cir. 2012) (quoting *Amgen*, 580 F.3d at 1370). "The party asserting anticipation bears the burden of proving that the process limitations do not result in an invention distinguishable from the prior art." *Cubist Pharms., Inc. v. Hospira, Inc.*, 75 F. Supp. 3d 641, 668 (D. Del. 2014) (citing *Amgen*, 580 F.3d at 1370), *aff'd*, 805 F.3d 1112 (Fed. Cir. 2015).

2. Findings of Fact

1. The priority date of the '066 patent is December 17, 2007.

2. Treprostinil is also known as UT-15 or treprostinil free acid. (DTX 258 at 1; DTX 674 at 4; Tr. at 408:16-17, 459:5-6, 461:5-6 (Winkler); Tr. at 742:5-9 (Gonda)).

3. A 2004 *Journal of Organic Chemistry* article by Moriarty et al., in relevant part titled "Synthesis of UT-15 (Treprostinil)" ("Moriarty"), teaches the synthesis of 99.7% pure treprostinil free acid, via alkylation and hydrolysis.

4. Moriarty is prior art.

5. The UT-15 treprostinil taught by Moriarty is the same chemical structure as the treprostinil product of claims 1-3, 6, and 9 of the '066 patent.

6. The average purity of UTC's batches of UT-15 treprostinil made by Moriarty and the '066 process are the same: 99.7%.

7. There are no structural or functional differences between the UT-15 treprostinil taught by Moriarty and the treprostinil claimed in the '066 patent.

3. Conclusions of Law

Claims 1, 2, 3, 6, and 9 are product-by-process claims, which claim a "pharmaceutical composition[/product] comprising treprostinil or a pharmaceutically acceptable salt thereof." Liquidia argues that these claims are invalid because the claimed product is the same product previously disclosed in the prior art by the 2004 Moriarty publication.[14] (D.I. 406 at 3).

---

[14] UTC faults Liquidia for failing to assert Moriarty as a § 102(a) anticipating reference. (D.I. 413 at 14 & n.10). This argument misunderstands Liquidia's invalidity theory. Liquidia claims that Moriarty anticipates under product-by-process law, not that Moriarty anticipates the claimed process steps. UTC did not object to the admission of evidence relating to this anticipation theory at trial. Thus, UTC cannot now argue that Moriarty is not prior art because Liquidia failed to disclose it as such. UTC also (newly) argues that Liquidia has failed to show that Moriarty was enabled. (*Id.* at 15-16). However, it is UTC's burden to prove that Moriarty is not enabled. *Apple Inc. v. Corephotonics, Ltd.,* 861 F. App'x 443, 450 (Fed. Cir. 2021) (nonprecedential) ("[R]egardless of the forum, prior art patents and publications enjoy a presumption of enablement, and the patentee/applicant has the burden to prove nonenablement for such prior art."); *In re Antor Media Corp.,* 689 F.3d 1282, 1289 (Fed. Cir. 2012) ("[D]uring patent prosecution, an examiner is entitled to reject claims as anticipated by a prior art publication or patent without conducting an inquiry into whether or not that

The 2004 article published in the *Journal of Organic Chemistry* by Robert M. Moriarty et al., entitled, in relevant part, "Synthesis of UT-15 (Treprostinil)" ("Moriarty"), teaches the synthesis of treprostinil free acid by alkylation and hydrolysis of BTO. (DTX 258 at 8; Tr. at 461:17-25 (Winkler)). Liquidia argues that the treprostinil product claimed in the product-by-process claims is identical to the treprostinil free acid of Moriarty.

As a preliminary matter, UTC argues that Moriarty cannot invalidate the product-by-process claims because it only discloses treprostinil, not a "pharmaceutical composition[/product] comprising treprostinil." (DI 413 at 8-9). The '066 patent, however, makes no distinction between treprostinil and a pharmaceutical composition/product comprising treprostinil. The specification only describes the steps for synthesizing treprostinil or treprostinil salt. (*See* JTX 2 at 9:46-14:54 (Examples 1-5), 17:23 (Example 6, step 51, final yield is "UT-15"); *see also id.* at 5:57-59 ("The present invention provides for a process for producing treprostinil and other prostacyclin derivatives and novel intermediate compounds useful in the process.")). There is no description of combining treprostinil or treprostinil salt with excipients. Thus, a POSA reading the '066 patent specification would understand that treprostinil is a "pharmaceutical composition[/product] comprising treprostinil." This reading is confirmed by the testimony of both parties' experts. (Tr. at 104:22-105:8 (Nuckolls) (stating that the pharmaceutical composition in claim 1 "could be Treprostinil or the pharmaceutically acceptable [salt

---

prior art reference is enabling. As long as an examiner makes a proper prima facie case of anticipation . . . , the burden shifts to the applicant to submit rebuttal evidence of nonenablement."). UTC has failed to submit such evidence.

thereof]"); Tr. at 462:15-24 (Winkler) (confirming that the product claimed by the product-by-process claims "could just be Treprostinil")).

Liquidia's expert Dr. Winkler testified that the UT-15 treprostinil disclosed in Moriarty and the '066 treprostinil were structurally and functionally the same. (Tr. at 457:6-480:2 (Winkler)). Specifically, the UT-15 treprostinil disclosed in Moriarty has the same chemical structure as the treprostinil product of claims 1, 2, 3, 6, and 9. (Tr. at 462:25-463:2, 467:3-5 (Winkler). *Compare* DTX 258 at 3 (depicting the chemical structure of UT-15 treprostinil as compound 7), *with* JTX 2 at 14:20-30 (depicting the chemical structure of treprostinil)). Claims 1, 2, 3, 6, and 9 do not claim any purity percentage, impurity profile, or commercial scale production.[15] (Tr. at 460:8-16 (Winkler)). The specification discloses that the treprostinil generated by the claimed process has a purity ranging from 99.7% to 99.9%. (JTX 2 at 14:55-65). The patent further advises, "In one embodiment, the purity of [treprostinil free acid] is at least 90.0%, 95.0%, 99.0%, 99.5%." (*Id.* at 9:22-23). The UT-15 treprostinil disclosed in Moriarty has a purity of

[15] UTC argues that the claim limitation requiring that the "level of one or more impurities found in the starting batch of treprostinil is lower in the pharmaceutical composition" defines the claimed product. (D.I. 413 at 7-8 (citing *In re Nordt Dev. Co.,* 881 F.3d 1371, 1376 (Fed. Cir. 2018))). I disagree. This impurities limitation is a process limitation that requires comparing the level of certain process impurities in the starting batch of treprostinil and the pharmaceutical composition, as shown in the infringement analysis above. This limitation merely describes the process and does not impart any structural or functional differences in the claimed pharmaceutical composition (as shown in Dr. Winkler's analysis discussed *infra*). *See In re Nordt,* 881 F.3d at 1375-76; *Greenliant,* 692 F.3d at 1268-69.

99.7%, which falls within the disclosures of the '066 patent specification. (DTX 258 at 13; Tr. at 462:9-14 (Winkler)).

Dr. Winkler also testified that UTC manufactured UT-15 treprostinil according to both processes. (Tr. at 463:20-22 (Winkler)). He testified that UTC used the Moriarty process in Chicago starting in 1997,[16] and in 2007, UTC moved the manufacturing process to Silver Spring, Maryland and changed to the '066 process. (Tr. at 464:15-465:2 (Winkler) (citing DTX 627A); Tr. at 546:1-4 (Batra); DTX 619). UTC told the FDA that the products made by both processes were the "same" and "equivalent." (DTX 70 at 3 ("[T]he lots of treprostinil API produced by the new process in Silver Spring are of the same high quality and purity as the commercial lots of API produced by the existing process at the Chicago facility."); DTX 619 at 10 ("The release data for the drug substance batch prepared by the revised route of synthesis indicate that it is of equivalent

[16] UTC argues that Dr. Winkler failed to show that UTC's former Chicago process was the same process disclosed in Moriarty. (D.I. 413 at 17-19). In reaching this conclusion, Dr. Winkler compared the Moriarty paper and the description of the Chicago process and determined that they recited the same reactions. (Tr. at 519:18-22,520:9-21 (Winkler)). Dr. Winkler also relied on one of the inventors, Dr. Batra, who testified that "Moriarty's process" "might be one of the terms" used to describe the Chicago process. (Tr. at 546:5-10 (Batra); *see also* JTX 2 at 1:28-31 ("Treprostinil, and other prostacyclin derivatives have been prepared as described in Moriarty . . . .")). No UTC witness disputed Dr. Winkler's statement that the Moriarty process was used in Chicago. In fact, UTC's witnesses relied on documents comparing the Chicago and Silver Spring products to demonstrate a structural difference. (*See* Tr. at 783:21-786:17 (Bunce); Tr. at 793:16-794:12, 799:4-802:19 (Walsh)). I therefore credit Dr. Winkler's testimony that the "Chicago process" and "Moriarty process" are the same.

quality to the batches produced by the current synthetic route, particularly with respect to the assay and purity profile."); DTX 646 at 4-5 ("[T]he simplified chemical synthesis of treprostinil will provide API that meets the same acceptance criteria as API obtained from the 20-step chemical synthesis, with a very similar impurity profile and similar acceptance criteria.")).

UTC used both processes to make treprostinil free acid for its drug Remodulin®. (Tr. at 467:17-468:3 (Winkler); Tr. at 545:7-19 (Batra); JTX 2 (titled "Process to Prepare Treprostinil, The Active Ingredient in Remodulin®")). UTC never represented to the FDA that the UT-15 treprostinil made according to the '066 patent in Silver Spring was safer, less toxic, or purer than the UT-15 treprostinil made according to Moriarty in Chicago. (Tr. at 469:7-14, 478:23-479:21 (Winkler)). Based on this, Dr. Winkler concluded that a POSA would understand there not to be any "efficacy, toxicity," or "biological activity" differences between the treprostinil made according to Moriarty and the '066 treprostinil. (Tr. at 479:12-21 (Winkler)).

Dr. Winkler further testified that UTC had identical specification limits (with respect to unidentified impurities, identified impurities, and total related substances) on allowable impurities between the two processes' products. (Tr. at 469:15-471:23 (Winkler). *Compare* DTX 151 at 1 (Silver Spring Product Certificate of Analysis from 2020), *and* DTX 627A at 5-6 (Silver Spring Process Optimization Batches Release Testing Data), *with* DTX 627A at 7 (Chicago Release Testing Data)). UTC increased its purity assay range from 97-101% (Chicago) to 98-102% (Silver Spring). (Tr. at 784:23-786:9 (Bunce); DTX 70 at 3; DTX 151 at 1; DTX 627A at 7). But Dr. Winkler testified that the purity of 96 batches of treprostinil made by the Chicago process

was 98.9%-100.3%, within both the 97-101% and 98-102% ranges. (Tr. at 470:21-473:5 (Winkler)). Dr. Winkler testified, and UTC did not refute, that the average purity of UTC's batches of UT-15 treprostinil made by the Chicago process and the Silver Spring process were the same: 99.7%. (Tr. at 473:16-477:18 (Winkler) (relying on the purity data submitted during the IPR for UTC's U.S. Patent No. 8,497,393 (DTX 664 at App. A ("Sample of product of Moriarty process")))).

No UTC expert or fact witness rebutted Dr. Winkler's opinions or provided testimony identifying any structural or functional difference between the Moriarty treprostinil free acid and the claimed treprostinil free acid product/composition. UTC only provided evidence relating to the functional and structural differences between the Moriarty treprostinil free acid and the claimed treprostinil salt product/composition. Dr. Walsh (inventor and former UTC employee) testified that the '066 process greatly reduced the 3AU90 impurity (an isomer of treprostinil) as compared to UTC's former Chicago process. (Tr. at 793:2-794:5, 795:12-796:12, 797:11-802:19 (Walsh)). Dr. Walsh, however, did not compare the Moriarty treprostinil free acid prepared in Chicago and the claimed treprostinil free acid product/composition. Instead, he compared the treprostinil free acid prepared at the Chicago facility and the treprostinil diethanolamine salt prepared by the '066 process. (Tr. at 803:1-12 (Walsh)). Dr. Walsh confirmed that treprostinil diethanolamine salt is a different compound from treprostinil free acid. (Tr. at 804:17-19 (Walsh)). Thus, Dr. Walsh's testimony fails to identify any structural or functional differences between the treprostinil products.

UTC also argues that the '066 patent's "capability for making a pharmaceutical composition from trepros-

tinil salt that had been stored at ambient temperature is novel over the prior art." (D.I. 413 at 24). UTC is improperly focusing on the process limitations of the claims. The storage and stability limitations in claims 6 and 9 relate to the intermediate salt generated during the process steps, not the final composition/ product. The claims do not cover any stability or storage of the final treprostinil product. Nor is this "capability" a structural or functional difference which appears in the claimed product. Instead, UTC admitted that the claimed treprostinil free acid was not stable at room temperature, which presents no improvement over the Moriarty UT-15 treprostinil. (Tr. at 964:19-965:7 (UTC Closing)).

The product-by-process claims recite a "pharmaceutical composition[/product] comprising treprostinil *or* a pharmaceutically acceptable salt thereof." Thus, if the treprostinil product is anticipated, then the claims are invalid, regardless of whether the treprostinil salt is anticipated. *See Brown v. 3M*, 265 F.3d 1349,1351 (Fed. Cir. 2001) ("When a claim covers several structures or compositions, either generically or as alternatives, the claim is deemed anticipated if any of the structures or compositions within the scope of the claim is known in the prior art."). UTC has not provided any evidence or expert testimony which compares the claimed treprostinil free acid to the Moriarty UT-15 treprostinil, instead choosing to focus on the claimed treprostinil salt. Accordingly, there is no record evidence that contradicts Dr. Winkler's testimony that the claimed treprostinil product and Moriarty UT-15 treprostinil are the same.

Liquidia has shown by clear and convincing evidence that the claimed Treprostinil product is functionally and structurally the same as the UT-15 treprostinil

disclosed in Moriarty. Thus, I find that claims 1, 2, 3, 6, and 9 of the '066 patent are invalid as anticipated.

B. Written Description (Claims 1, 2, 3, and 6)

1. Legal Standard

The written description requirement contained in 35 U.S.C. § 112 requires that the specification "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (alteration in original). "In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "When determining whether a specification contains adequate written description, one must make an 'objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.'" *Bos. Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011) (quoting *Ariad*, 598 F.3d at 1351).

The written description inquiry is a question of fact. *Ariad*, 598 F.3d at 1351. "A party must prove invalidity for lack of written description by clear and convincing evidence." *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 682 (Fed. Cir. 2015).

2. Findings of Fact

1. A POSA reading the '066 patent specification would have understood that the alkylation step results in a light brown material, the hydrolysis step results in a pale yellow material, and the salt formation step results in an off-white material, indicating the gener-

ation and lowering of impurities from the alkylation and hydrolysis steps.

2. TLC may be used to qualitatively see the presence of impurities generated as the reaction proceeds. A POSA would have understood from the specification disclosure that monitoring the progress of a reaction by TLC would include identification of impurities generated during the reaction step.

3. Conclusions of Law

Liquidia asserts that there is no written description support for claim l's limitation requiring that "a level of one or more impurities found in the starting batch of treprostinil is lower in the pharmaceutical composition." Claim 1 further requires "a starting batch of treprostinil having one or more impurities resulting from prior alkylation and hydrolysis steps . . . wherein said alkylation is alkylation of benzindene triol."

The specification provides adequate written description support for the impurities limitation. Specifically, the specification provides, "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." (JTX 2 at 17:29-32). Liquidia argues that this passage does not provide adequate written description support because it does not specify whether the impurities that are reduced are from the alkylation and hydrolysis of BTO. (D.I. 406 at 12-13). This argument, however, is based on Liquidia's narrow claim construction, which I rejected above. A POSA would understand that claim 1 encompasses any impurity generated during the alkylation and hydrolysis steps. Thus, based on this language in the specification, a POSA would under-

stand that the inventors were in possession of the impurities limitation. (*See* Tr. at 818:1-22 (Scheidt)).

Yet, Liquidia argues that since the specification does not report the level of impurities generated during the alkylation and hydrolysis steps, the '066 patent does not provide any written description of a "level of one or more impurities found in the starting batch of treprostinil" to compare to the pharmaceutical composition. (Tr. at 480:25-482:7 (Winkler); *see* JTX 2 at 9:49-10:37, 10:40-11:49). Liquidia argues, "[T]here is insufficient data and information in the specification of the '066 patent for a POSA to make such a comparison as claimed." (D.I. 406 at 10). This argument is not a written description argument; it might be an enablement argument. The specification need not report quantitative impurities data to provide written description support. While the '066 patent does not disclose quantitative impurities measurements, it provides qualitative measures that would alert a POSA to the generation and reduction of impurities as claimed.

As UTC's expert Dr. Scheidt testified, the '066 patent describes that the alkylation step results in a light brown material, the hydrolysis step results in a pale yellow material (i.e., the starting batch of treprostinil), and the salt formation step results in an off-white material. (Tr. at 810:13-811:1 (Scheidt); JTX 2 at 9:49-10:37 (alkylation of benzindene triol), 10:40-11:49 (hydrolysis of benzindene nitrile), 14:1-54 (conversion of treprostinil diethanolamine salt to treprostinil)). Dr. Scheidt credibly testified that a POSA would understand that these color changes indicate the generation and lowering of impurities from the alkylation and hydrolysis steps. (Tr. at 811:17-812:5, 817:5-25, 819:7-18 (Scheidt); *see also* Tr. at 484:2-8, 488:3-15, 532:16-24 (Winkler) (acknowledging that changes in color can

indicate the presence of an impurity)). Liquidia faults Dr. Scheidt's analysis because the color differences do not show the specific impurity or the amount of impurity removed. (D.I. 406 at 11). This argument, however, relies on Liquidia's erroneous construction. A POSA would understand that claim 1 encompasses any impurity generated during the alkylation and hydrolysis steps. Further, the claim simply requires the lowering of the impurities, so the specification need not disclose the specific amount of impurities removed to provide adequate written description support.

The '066 patent specification also provides that the progress of the alkylation and hydrolysis reactions were monitored by thin layer chromatography ("TLC"). (JTX 2 at 10:30-32, 11:13-16). TLC may be used to qualitatively see the presence of impurities generated as the reaction proceeds. (Tr. at 812:9-814:16 (Scheidt)). Although the patent does not disclose the use of TLC to identify or measure impurities, I credit Dr. Scheidt's testimony that a POSA would understand that the TLC would include identification of impurities generated during the reaction steps. (*Id.*).

I find that these disclosures in the '066 patent "reasonably convey to those skilled in the art that the inventor had possession" of the impurities limitation.[17]

---

[17] Liquidia relies on inventor testimony to show that the inventors did not possess the impurities limitation. (D.I. 406 at 10, 12-13). This inventor testimony does not alter my conclusion. The test for written description "requires an objective inquiry into the four corners of the specification." *Ariad,* 598 F.3d at 1351. The disclosures in the '066 patent reasonably convey possession of the claimed impurities limitation. I therefore see no reason to look beyond the four corners of the specification. *See Biogen Intl GmbH v. Mylan Pharms. Inc.,* 28 F.4th 1194, 1202 (Fed. Cir. 2022) (Lourie, J., dissenting from the denial of the petition for rehearing en banc) ("Where the disclosure in a patent's specification plainly

Ariad, 598 F.3d at 1351. Liquidia has not proven by clear and convincing evidence that claims 1, 2, 3, and 6 of the '066 patent are invalid for lack of written description.

IV. INFRINGEMENT OF THE '793 PATENT

A. Legal Standard

"Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b); *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1363 (Fed. Cir. 2003). To prevail on a claim of induced infringement, the plaintiff must show (1) "that there has been direct infringement," and (2) "that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement." *Enplas Display Device Corp. v. Seoul Semiconductor Co.*, 909 F.3d 398, 407 (Fed. Cir. 2018) (internal citation omitted).

In a Hatch-Waxman case, a plaintiff "can satisfy its burden to prove the predicate direct infringement by showing that if the proposed []NDA product were marketed, it would infringe the [asserted claims]." *Vanda Pharms. Inc. v. W.-Ward Pharms. Intl Ltd.*, 887 F.3d 1117, 1130 (Fed. Cir. 2018). For method-of-treatment patents, if an NDA applicant's "proposed label instructs users to perform the patented method[,] . . . the proposed label may provide evidence of [the NDA applicant's] affirmative intent to induce infringement." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010). In that setting, the Federal Circuit has

---

corresponds to what is claimed, extrinsic evidence should not be used to cast doubt on the meaning of what is disclosed."). Even if I were to consider the inventor testimony, I would find that it does not provide clear and convincing evidence that the claims lack written description.

explained, "The label must encourage, recommend, or promote infringement." *Takeda Pharms. USA., Inc. v. W-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015). Evidence that a proposed label will "inevitably lead some consumers to practice the claimed method" can suffice to support a finding of specific intent to induce infringement. *AstraZeneca,* 633 F.3d at 1060.

B. Asserted Claims of the '793 patent

1. A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

4. The method of claim 1, wherein the inhalation device is a dry powder inhaler.

6. The method of claim 4, wherein the formulation is a powder.

7. The method of claim 6, wherein the powder comprises particles less than 5 micrometers in diameter.

8. The method of claim 1, wherein the formulation contains no metacresol.

C. Findings of Fact

1. A POSA would have a medical degree with a specialty in pulmonology or cardiology, plus at least two years of experience treating patients with PH as an attending, including with inhaled therapies, or equivalent degree or experience.

2. LIQ861 is administered "3 to 5 times per day." Each administration is a single event dose.

3. LIQ861 is administered in a single event dose that is therapeutically effective.

4. Treprostinil is a vasodilator that reduces vasoconstriction in the pulmonary vasculature, causing vasodilation (widening of vasculature) and reduction of pulmonary artery pressure ("PAP") and pulmonary vascular resistance ("PVR").

5. A single administration of treprostinil will improve a patient's hemodynamics.

6. A single administration of LIQ861 will have positive hemodynamic effects, i.e., reduce PAP and PVR.

7. Liquidia has knowledge of the '793 patent.

8. Liquidia's proposed LIQ861 label teaches all elements of the asserted claims of the '793 patent.

9. Knowing that the method of administering LIQ861 is infringing, Liquidia will encourage, recommend, and promote use of LIQ861 in an infringing manner, including by providing the label, patient instructions, and additional training and other information to physicians and patients.

D. Conclusions of Law

1. Act of Direct Infringement

Liquidia argues that UTC has failed to prove that LIQ861 is administered in "a therapeutically effective single event dose," as required by claim 1 and therefore every asserted claim.[18]

---

[18] Liquidia does not dispute infringement of the remaining limitations in claims 1, 4, 6, 7, and 8. (*See* D.I. 411 at 12-17).

Liquidia argues that claim 1 is limited to one single event dose per day rather than multiple doses per day. (D.I. 411 at 13). Liquidia reasons that claim 1 recites a "single event dose" rather than simply a "dose." (*Id.*). Liquidia's argument lacks merit. The term "single" modifies "event," not "dose." The experts agree that "single event dose" refers to a dose that is delivered in a single treatment session (i.e., a "single event"), including a session that involves multiple breaths. (Tr. at 675:4-15 (Waxman); Tr. at 704:25-705:9 (Hill)).

The claim language does not limit the number of single event doses per day. The claim recites the administration of "a" single event dose. The Federal Circuit "has repeatedly emphasized that an indefinite article 'a' or 'an' in patent parlance carries the meaning of 'one or more' in open-ended claims containing the transitional phrase 'comprising." *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000). There is no language in the claims or specification that necessitates a departure from this general rule. *See Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342-43 (Fed. Cir. 2008) ("An exception to the general rule that 'a' or 'an' means more than one only arises where the language of the claims themselves, the specification, or the prosecution history necessitate a departure from the rule.").

The specification is consistent with the general meaning of "a." The specification expressly states, "Treprostinil can be administered a single time per day or several times per day." (JTX 3 at 8:1-2). Further, based on treprostinil's three- to four-hour half-life, a POSA would understand that a patient would need to receive more than one single event dose per day. (Tr. at 704:9-24 (Hill)). Accordingly, I conclude that the scope of claim 1 is not limited to one single event dose per

day. I find that LIQ861 is administered in a single event dose. The proposed LIQ861 label states that LIQ861 "should be administered 3 to 5 times per day." (PTX 469 at 4). Each administration is a single event dose. (*See* Tr. at 676:15-20 (Waxman); Tr. at 705:1-9, 707:5-22 (Hill)).

The parties agree that claim 1 requires that each "single event dose" be "therapeutically effective." (Tr. at 651:5-22 (Waxman); Tr. at 683:2-9 (Hill)). The parties, however, dispute the plain and ordinary meaning of "therapeutically effective." UTC's expert Dr. Waxman testified that a therapeutically effective single event dose is one that causes a positive change in a patient's hemodynamics—i.e., "a therapeutically effective dose should cause a reduction in pulmonary artery pressure and cause a reduction in pulmonary vascular resistance." (Tr. at 651:3-22 (Waxman)). In contrast, Liquidia's expert Dr. Hill testified that a single event dose is therapeutically effective when it causes an "improvement in symptoms, in function, and/or in survival." (Tr. at 685:15-21 (Hill)). Based on the teachings of the '793 patent, I agree with Dr. Waxman that a POSA would understand the plain and ordinary meaning of "therapeutically effective single event dose" to be a dose given in a single treatment session that causes an improvement in a patient's hemodynamics (reduced PAP or PVR).

The examples in the specification studied the hemodynamic effects after a single event dose of treprostinil. (*See, e.g.*, JTX 3 at 8:57-18:11; 9:11-21 ("Pulmonary hemodynamics and blood gases were measured at defined time points . . . . [Inhaled treprostinil sodium] doses of 30 µg, 45 µg and 60 µg reduced pulmonary vascular resistance (PVR) . . . . Reduction of PVR by a single inhalation of the two higher doses outlasted the

observation period of 120 minutes."); 11:62-66 ("The application of an effective amount of treprostinil in only few or even one single breath was achieved with a highly concentrated treprostinil sodium solution.")). The examples in the patent do not report long-term measures like patient survival rate. (*See* Tr. at 702:12-20 (Hill)). A POSA reading the '793 patent would thus understand that a single event dose is therapeutically effective when it improves a patient's hemodynamics.

I find that UTC has proven by a preponderance of the evidence that LIQ861 is administered in a therapeutically effective single event dose. Treprostinil is a vasodilator that reduces vasoconstriction in the pulmonary vasculature, causing vasodilation (widening of vasculature) and reduction of PAP and PVR. (Tr. at 650:20-25 (Waxman); Tr. at 700:13-17 (Hill) (acknowledging that "the goal of using a vasodilator such as Treprostinil is to reduce the pulmonary arterial pressure and/or pulmonary vascular resistance")). Both experts agree that the '793 patent shows that the claimed single-event dosing of treprostinil improves a patient's hemodynamics. (Tr. at 637:22-25 (Waxman); Tr. at 702:1-4 (Hill) (agreeing that the '793 patent shows hemodynamic effectiveness from treprostinil); *see also* Tr. at 702:5-11 (Hill) (agreeing that on average, "a single administration of Treprostinil to someone suffering from pulmonary hypertension results in a beneficial reduction of pulmonary arterial pressure and/or vascular resistance")).

Liquidia argues that these disclosures are not evidence that a single event dose of LIQ861 will have hemodynamic effects because LIQ861 is administered in a completely different form than Tyvaso®. (D.I. 411 at 15). LIQ861 is a dry powder formulation, while Tyvaso® is a liquid formulation delivered to the

patient via a nebulizer. (Tr. at 696:6-12 (Hill)). But, as Dr. Hill acknowledged, Tyvaso® and LIQ861 involve the same molecule (treprostinil). (Tr. at 711:4-6 (Hill)). Dr. Hill testified that, because they involve the same molecule, he would expect Tyvaso® and LIQ861 to have similar effects on PAP and PVR. (Tr. at 711:4-11 (Hill); *see also* Tr. at 694:20-695:2 (Hill) (after a single event dose of LIQ861, "There might be a transient improvement in hemodynamics. There might be no effect on the hemodynamics, but in the longer term, the effect would dissipate within hours, and you would expect no therapeutic effect beyond those first few hours.")). In fact, Liquidia relied on Tyvaso®'s safety and efficacy data in its NDA. (PTX 573 at 7 ("The NDA for LIQ861 inhalational powder . . . rel[ies] on the FDA's previous finding of safety and effectiveness for Tyvaso, the selected reference listed drug (RLD) for demonstration of the effectiveness of treprostinil in the treatment of PAH."); *see also* PTX 1213 (demonstrating that LIQ861 and Tyvaso® have the same bioavailability)).

UTC's evidence shows that a single administration of treprostinil will improve a patient's hemodynamics, and thus proves by a preponderance of the evidence that a single administration of LIQ861 at the claimed doses will improve a patient's hemodynamics. I therefore find that UTC has proven by a preponderance of the evidence that the administration of LIQ861 will directly infringe claims 1,4,6,7, and 8 of the '793 patent.

2. Specific Intent to Induce Infringement

Liquidia argues that it lacks specific intent to induce infringement because the proposed LIQ861 label does not encourage administration of a "therapeutically effective single event dose." (D.I. 411 at 16-17). Liquidia argues that the label does not "instruct[] that LIQ861

produces hemodynamic changes after a single event dose" because the label does not contain any hemodynamic data or instruction to doctors to measure hemodynamic changes after a single event dose. (*Id.*). The label, however, does not need to provide hemodynamic data to induce infringement. It just needs to instruct doctors and patients to administer a single event dose that is therapeutically effective. *See AstraZeneca*, 633 F.3d at 1060 (finding that evidence that a proposed label will "inevitably lead some consumers to practice the claimed method" can suffice to support a finding of intent to induce infringement). The LIQ861 label does so by instructing doctors and patients to administer LIQ861 "3 to 5 times per day" at the claimed doses. (*See* PTX 469 at 1 6). As discussed above, UTC has proven that a single administration of LIQ861 will be therapeutically effective. Thus, the label's instructions will "inevitably lead" to the administration of a "therapeutically effective single event dose."[19] UTC has met its burden to show intent to induce infringement.

I therefore find that UTC has proven by a preponderance of the evidence that Liquidia will induce infringement of claims 1, 4, 6, 7, and 8 of the '793 patent.

On July 19, 2022, the PTAB issued a Final Written Decision in the IPR of the '793 patent, invalidating all claims of the '793 patent as obvious. *Liquidia Techs.*,

---

[19] Liquidia also argues that the label does not encourage patients to use LIQ861 as a "single event dose" because the label instructs doctors and patients to administer LIQ861 "3 to 5 times per day." (D.I. 411 at 16-17). But, as discussed above, claim 1 is not limited to one single event dose per day. The LIQ861 label instructs and encourages the administration of LIQ861 as a "single event dose."

Inc. v. United Therapeutics Corp., No. IPR2021-00406, 2022 WL 2820717 (P.T.A.B. July 19, 2022). Liquidia argues that it therefore cannot be liable for induced infringement under the Supreme Court's decision in *Commil*. (D.I. 427).

In *Commil*, the Supreme Court held that an accused infringer's "belief regarding patent validity" is not a defense to a claim of induced infringement. *Commil USA, LLC v. Cisco Sys., Inc.*, 575 U.S. 632, 642 (2015). The Supreme Court also stated, "[I]f . . . an act that would have been an infringement or an inducement to infringe pertains to a patent that is shown to be invalid, there is no patent to be infringed." *Id.* at 644. The Supreme Court further explained, "An accused infringer can, of course, attempt to prove that the patent in suit is invalid; if the patent is indeed invalid, and shown to be so under proper procedures, there is no liability." *Id.* The Supreme Court never stated, however, that a PTAB decision invalidating patent claims in an IPR will preclude liability before it becomes final and nonappealable. *Id.* at 644-45. The Court simply stated that an IPR proceeding is one procedure through which an accused infringer can pursue an invalidity challenge. *Id.* at 645. I therefore do not think that *Commil* compels this Court to treat the '793 patent as invalid for purposes of assessing Liquidia's induced infringement. (*See* D.I. 427 at 1).

Instead, the Federal Circuit has indicated that an IPR decision does not have collateral estoppel effect until that decision is affirmed or the parties waive their appeal rights. *See XY, LLC v. Trans Ova Genetics*, 890 F.3d 1282, 1294 (Fed. Cir. 2018) ("[A]n affirmance of an invalidity finding, whether from a district court or the Board, has a collateral estoppel effect on all pending or co-pending actions."); *Papst Licensing GMBH*

& Co. KG v. Samsung Elecs. Am., Inc., 924 F.3d 1243, 1249 (Fed. Cir. 2019) (finding IPR decision became final after appeals were voluntarily dismissed). Further, the PTAB's FWD does not cancel claims. The claims are cancelled when the Director issues a certificate confirming unpatentability, which only occurs after "the time for appeal has expired or any appeal has terminated." 35 U.S.C. § 318(b); *see also Fresenius USA, Inc. v. Baxter Intl, Inc.*, 721 F.3d 1330, 1346 (Fed. Cir. 2013) ("[I]t could hardly be clearer that Congress meant for cancellation to terminate pending suits.").

Therefore, I find that the PTAB's decision—which is not yet final—has no impact on my finding of induced infringement.

V. INVALIDITY OF THE '793 PATENT

A. Legal Standard

A patent's specification must enable the claimed invention. *In re Cortright*, 165 F.3d 1353, 1356 (Fed. Cir. 1999). For a patent claim to be enabled, "The specification shall contain a written description of the invention, and of the manner and process of making and using it. in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same[.]" 35 U.S.C. § 112(a). "The enablement requirement is met where one skilled in the art, having read the specification, could practice the invention without 'undue experimentation.' *Streck, Inc. v. Rsch. & Diagnostic Sys., Inc.*, 665 F.3d 1269, 1288 (Fed. Cir. 2012) (citation omitted). Factors for assessing whether a disclosure would require undue experimentation include:

(1) the quantity of experimentation necessary,
(2) the amount of direction or guidance pre-

> sented, (3) the presence or absence of working examples. (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art. (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

"Enablement is a question of law based on underlying facts." *Wyeth & Cordis Corp. v. Abbott Lab'ys*, 720 F.3d 1380, 1384 (Fed. Cir. 2013). The party challenging validity must prove lack of enablement by clear and convincing evidence. *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1336 (Fed. Cir. 2013).

B. Findings of Fact

1. The '793 patent has a priority date of May 15,2006.

2. With respect to treating PH, a POSA would have a medical degree with a specialty in pulmonology or cardiology, plus at least two years of experience treating patients with PH as an attending, including with inhaled therapies, or equivalent degree or experience. With respect to inhaled formulations used in treating PH, a POSA would have a Ph.D. in pharmaceutical science or a related discipline like chemistry or medicinal chemistry, plus two years of experience in pharmaceutical formulations, including inhaled products, or equivalents (e.g., an M.S. in the same fields, plus five years of experience).

3. A POSA would understand "treating pulmonary hypertension," as claimed, to encompass treating all five WHO Groups of pulmonary hypertension ("PH"), including both isolated Group 2 (also referred to as

isolated postcapillary Group 2) and pre- and postcapillary combined Group 2.

4. Treprostinil is a member of the family of compounds referred to as prostacyclins or prostacyclin analogs. (JTX 3 at 5:37-39; Tr. at 573:21-22 (Hill)). Prostacyclins dilate, or widen, the blood vessels of the lungs. (Tr. at 574:10-15 (Hill)).

5. A POSA would understand that the claimed administration of treprostinil vasodilates the pulmonary vasculature and reduces PAP and PVR, even in Group 2 PH patients.

6. The processes involved in developing dry powder formulations were well known as of 2006 and utilized routine techniques for both manufacturing and analysis.

7. Numerous dry powder inhaler ("DPI") devices were available by 2006.

8. By 2006 it was common for a POSA to develop a powder blend and then choose an available DPI for delivery of the powder formulation. Not all DPI devices need to be separately developed or specifically chosen for a given patient population.

9. Using well-known and routine techniques, Dr. Smyth prepared treprostinil free acid and treprostinil diethanolamine dry powder formulations that delivered doses within the claimed 15-90 μg range with three weeks of testing. Dr. Smyth's testing demonstrated that PH patients could effectively inhale these dry powder formulations using a DPI.

10. Selecting a suitable form of treprostinil was routine as of 2006. Methods for determining suitable forms, including salt forms, of a particular API were well known and routine for several decades prior to 2006.

11. Lactose was the only FDA-approved carrier in 2006 and was also the most common excipient for use in dry powder inhalers.

12. The Maillard reaction was well known and understood as of 2006. A POSA would have understood how to monitor any Maillard reaction between treprostinil diethanolamine and lactose.

13. Meyer (PTX 1980) was available before the priority date and discloses that PH patients were able to obtain maximum inspiratory efforts of 5.2 kPa in females and 6.8 kPa in males, which is enough to use a DPI.

C. Conclusions of Law

1. Enablement of "Treating Pulmonary Hypertension"

The asserted claims of the '793 patent recite: "A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof . . . ." Liquidia argues that the full scope of "treating pulmonary hypertension" is not enabled.

Before addressing enablement, I must first resolve the parties' claim construction dispute. Liquidia asserts that the phrase "treating pulmonary hypertension" encompasses treating all five WHO groups of pulmonary hypertension ("PH"). (D.I. 406 at 14). UTC argues that the claims are limited to treating precapillary PH. (D.I. 413 at 29-30).

PH refers to abnormally high blood pressure in the lungs. (Tr. at 562:13-14, 563:18-21 (Hill); Tr. at 629:9-630:1, 677:21-678:7 (Waxman)). PH includes a range of

conditions classified in five different WHO groups: Group 1, pulmonary arterial hypertension; Group 2, pulmonary venous hypertension, i.e., PH related to left heart disease; Group 3, PH associated with disorders damaging the lungs; Group 4, PH caused by chronic thrombotic or embolic disease, including chronic blood clots in the lungs; and Group 5, a miscellaneous category for conditions that do not fit well into the other four groups. (JTX 3 at 1:41-46; Tr. at 564:19-566:7, 575:22-576:4 (Hill); Tr. at 609:18-610:11 (Rubin); DTX 385 at 2).

PH Groups 1,3, and 4 are classified as "precapillary" PH as they are characterized by conditions affecting the pulmonary arteries or precapillary vessels. (Tr. at 564:18-566:4, 591:24-592:1 (Hill)). In contrast, the high blood pressure in the lungs of Group 2 PH patients has a different underlying cause. Defects in the left side of the heart cause elevated pressure in the postcapillary veins which reflects back as high pressure in the pulmonary arteries. (Tr. at 565:4-16, 571:17-24 (Hill)). Because the left heart is downstream (in terms of blood flow) of the pulmonary capillaries, Group 2 PH is sometimes referred to as "postcapillary" PH. (Tr. at 564:5-17, 565:4-16 (Hill); Tr. at 630:10-17 (Waxman)). Group 2 PH patients can suffer from isolated postcapillary PH or combined pre- and postcapillary PH. (Tr. at 571:10-14 (Hill); Tr. at 659:8-14 (Waxman)). In combined Group 2 PH patients, the precapillary vessels undergo changes similar to those in precapillary Group 1 PH. (Tr. at 571:10-572:8 (Hill)).

Because the cause of postcapillary PH is the left heart, not precapillary resistance, the "mainstay of treatment" by POSAs for postcapillary PH is a diuretic, not a vasodilator like treprostinil. (Tr. at 636:1-5 (Waxman); *see also* Tr. at 587:5-588:5, 600:2-9 (Hill)

(stating that treating postcapillary PH patients with a vasodilator would be "stupid" because vasodilation can lead to pulmonary edema)).

Claim 1 requires "treating pulmonary hypertension comprising administering . . . treprostinil," a vasodilator. Based on this language, UTC argues that a POSA would understand claim 1 to be limited to "treating varieties of PH where using a vasodilator addresses the cause of the disease." (D.I. 413 at 30). Thus, because both experts agree that a POSA would not treat postcapillary PH with treprostinil, UTC contends that a POSA would read the claim to be limited to the treatment of precapillary PH.

This expert testimony, however, is no substitute for the clear disclosures in the '793 patent specification. The specification expressly includes all five Groups when describing "pulmonary hypertension." (JTX 3 at 1:41-45 ("Pulmonary hypertension may occur due to various reasons and the different entities of pulmonary hypertension were classified based on clinical and pathological grounds in 5 categories according to the latest WHO convention." (citing DTX 385)); *see also id.* at 1:37-38 ("Generally, pulmonary hypertension is defined through observations of pressures above the normal range . . . ."). The specification does not contain any disclosures which limit the scope of "pulmonary hypertension" to any particular subset of PH patients. Instead, the specification refers to both "precapillary pulmonary hypertension" and "pulmonary hypertension," demonstrating that the inventors viewed precapillary PH as a subset of the broadly claimed "pulmonary hypertension." (*Id.* at 9:36-37, 12:64-65,16:64-65).

Based on these clear disclosures in the specification, I conclude that the scope of "treating pulmonary hypertension" includes treating all five Groups of PH.

Returning to enablement, Liquidia argues that it would require undue experimentation to practice the full scope of the claimed "treating pulmonary hypertension," specifically treating Group 2 PH patients. (D.I. 406 at 15-19). Dr. Hill testified that as of May 15,2006, a POSA would have had significant safety concerns about administering inhaled treprostinil to treat Group 2 PH patients. (Tr. at 592:3-593:18 (Hill)). Several studies have indicated that Group 1 PH therapies like prostacyclins could exacerbate symptoms in Group 2 PH patients. In the FIRST trial, patients with Group 2 PH were treated intravenously with the prostacyclin epoprostenol. (Tr. at 582:12-583:23 (Hill)). Because more people died in the epoprostenol treatment group than in the control group, the study was prematurely stopped. (Tr. at 583:4-13, 585:10-14,585:21-586:2 (Hill); DTX 358 at 1,8-9 ("[C]hronic epoprostenol infusion in severe left ventricular failure resulted in increased mortality rates and no evidence of improved quality of life."); *see also* DTX 385 at 2 (citing the FIRST study when noting "epoprostenol therapy in patients with pulmonary venous hypertension [Group 2 PH] can be harmful")).

The label for Ventavis® (iloprost), which was the only inhaled prostacyclin approved for treatment of Group 1 PH as of May 15,2006, similarly warned that treatment should be stopped if signs of pulmonary edema occur, as this may be a sign of pulmonary venous hypertension. (DTX 345 at 6; Tr. at 586:6-587:22 (Hill)). Dr. Hill testified that, based on this warning and the results of the FIRST trial, a POSA would have been extremely cautious about using intravenous and inhaled prostacyclins, like treprostinil, in Group 2 PH patients, as such use could create a potentially life-threatening situation in these patients. (Tr. at 587:5-588:5 (Hill)).

Prostacyclins dilate the precapillary vessels, which allows more blood to flow through the capillaries and into the pulmonary veins. (*Id.*). According to Dr. Hill, this increased blood flow "could increase the pulmonary venous pressure, the pressure filling the left heart, and that increase in the capillaries can cause leakage of fluid into the gas exchanging areas of the lungs, interfering with oxygenation and creating a potentially life-threatening situation." (*Id.*).

The experts agree that the '793 patent only describes treating Groups 1,3, and 4 PH, which are all precapillary. (*See* JTX 3 at 8:57-18:20; Tr. at 579:25-580:23, 590:25-592:2 (Hill); Tr. at 634:22-635:13 (Waxman)). Because there are no disclosures in the '793 patent or the prior art establishing the feasibility or safety of treating Group 2 PH patients with inhaled treprostinil, Dr. Hill concluded that a POSA would have had to conduct undue experimentation to treat Group 2 PH with treprostinil. (Tr. at 592:13-593:18 (Hill)). Specifically, a POSA would have had to "start at square one," conducting additional preclinical and clinical trials to determine whether the treprostinil formulation was safe and effective in treating Group 2 PH patients. (Tr. at 593:2-18 (Hill)).

I have no doubt that a physician would have certain safety concerns about treating Group 2 PH patients—particularly isolated Group 2 PH patients—with treprostinil. (*See* Tr. at 635:16-636:10 (Waxman)). But the fact that a POSA would have safety concerns does not necessarily show a lack of enablement. The claims do not require *"safely and effectively* treating pulmonary hypertension," as Liquidia seems to be arguing. The claims instead require "treating pulmonary hypertension comprising administering . . . a therapeutically

effective single event dose of a formulation comprising treprostinil."

As discussed above, a POSA would understand "a therapeutically effective single event dose" to be a dose given in a single treatment session that causes an improvement in a patient's hemodynamics (reduced PAP or PVR). Applying this construction, Liquidia has not shown by clear and convincing evidence that a POSA would have to conduct undue experimentation to practice the claimed method of treating PH.

There is no dispute that the '793 patent enables treatment of patients with Groups 1,3,4, and 5 PH. (*See* D.I. 406 at 16-17). The '793 patent describes the invention including the specific drug, conditions the invention is intended to treat (PH), dosages (15-90 μg), and mode and method of treatment (1-3 breaths by inhalation). (JTX 3 at 6:41-45, 7:7-12, 7:55-58, 7:64, 8:20-31, 18:1-6). The '793 patent also describes the improved hemodynamics that result from the use of the claimed invention, and the absence or reduction of side effects. (*Id.* at 8:57-18:11; Tr. at 637:22-638:3 (Waxman); Tr. at 702:1-11 (Hill)).

The record demonstrates that the claimed administration of treprostinil vasodilates the pulmonary vasculature and reduces pulmonary blood pressure, even in isolated Group 2 PH patients. (*See* Tr. at 582:11-19, 583:14-585:23, 587:5-588:5 (Hill); Tr. at 637:18-640:5 (Waxman); DTX 358). The FIRST study, involving Flolan® (epoprostenol), showed that treating isolated Group 2 PH patients with a prostacyclin had preliminary clinical evidence of benefit and a statistically significant acute hemodynamic improvement, including a reduction of mean PAP, wedge pressure, and PVR, and improvements in exercise duration and dyspnea score. (Tr. at 582:11-19,583:14-585:23 (Hill);

DTX 358 at 1,5-7). Thus, even with a risk of pulmonary edema, a POSA would understand that the claimed administration of Treprostinil would vasodilate the pulmonary vasculature, affect hemodynamics, and treat a patient's elevated pulmonary blood pressure, i.e., treat PH. (*Id.;* JTX 3 at 1:33-40, 2:13-15, 2:30-38; Tr. at 587:5-588:5 (Hill); Tr. at 637:18-640:5 (Waxman)).

Liquidia has thus failed to show by clear and convincing evidence that it would require undue experimentation for a POSA to use treprostinil to improve a patient's hemodynamics, i.e., to treat PH as claimed. The fact that a physician might be cautious and need to monitor the patient more closely when administering treprostinil to isolated Group 2 PH patients does not change this result.

I therefore find that Liquidia has failed to show by clear and convincing evidence that claims 1,4,6,7, and 8 of the '793 patent are invalid for lack of enablement.

2. Written Description of "Treating Pulmonary Hypertension"

Liquidia argues that the asserted claims of the '793 patent are invalid for lack of written description. Specifically, Liquidia contends that the '793 patent fails to convey with reasonable certainty that the inventors possessed the full scope of treating PH as claimed. Liquidia reasons that the '793 patent specification does not describe treating Group 2 PH patients with inhaled treprostinil and does not address the safety concerns that a POSA would have with respect to treating Group 2 PH patients with treprostinil. (D.I. 406 at 19). But just like its enablement argument, Liquidia's position seems to be based on the flawed premise that the claims require "a method of safely and effectively treating pulmonary hypertension."

As the Federal Circuit has explained, to satisfy the written description requirement, "An inventor need not prove that a claimed pharmaceutical compound actually achieves a certain result. But when the inventor expressly claims that result, our case law provides that such result must be supported by adequate disclosure in the specification." *Biogen Int'l GMBH v. Mylan Pharms. Inc.*, 18 F.4th 1333, 1343 (Fed. Cir. 2021) (cleaned up). The '793 patent claims require "treating pulmonary hypertension comprising administering . . . a therapeutically effective single event dose of a formulation comprising treprostinil." The only effectiveness that is claimed is "a therapeutically effective single event dose of . . . treprostinil." The '793 patent contains adequate written description support for this claimed result.

The '793 patent describes how administering inhaled treprostinil targets the lungs, dilates the blood vessels, and reduces blood pressure. (*See* JTX 3 at 2:29-43, 3:25-5:2, 5:13-36, 8:57-18:11; Tr. at 637:22-25 (Waxman); Tr. at 702:1-11 (Hill)). Even though a POSA might have safety concerns regarding the treatment of isolated Group 2 PH patients, a POSA would understand, based on these disclosures, that treprostinil would effectively vasodilate the pulmonary vasculature, affect hemodynamics, and treat a patient's elevated pulmonary blood pressure. (*Id.*). Accordingly, these disclosures "reasonably convey[] to those skilled in the art that the inventor had possession" of the full scope of treating PH as claimed.

I therefore find that Liquidia has failed to prove by clear and convincing evidence that claims 1, 4, 6, 7, and 8 of the '793 patent are invalid for lack of written description.

3. Written Description of Dry Powder Formulations and Dry Powder Inhaler

Claim 1 of the '793 patent recites using an inhaled "formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device." The parties agree that claim 1 encompasses inhaled liquid solutions delivered via nebulizers, soft mist inhalers, and metered dose inhalers, and dry powder formulations delivered via a dry powder inhaler ("DPI"). (*See* D.I. 406 at 21; D.I. 413 at 35). Further, dependent claims 4,6, and 7 specifically recite the use of a DPI and a powder formulation of treprostinil. Liquidia argues that the '793 patent does not provide adequate written description support for the claimed dry powder formulation of treprostinil or corresponding DPI suitable for treating PH patients. (D.I. 406 at 21).

The '793 patent specification provides, "The inhalation device can be also a dry powder inhaler. In such case, the respiratory drug is inhaled in solid formulation, usually in the form of a powder with particle size less than 10 micrometers in diameter or less than 5 micrometers in diameter." (JTX 3 at 7:22-26). Liquidia argues that this statement is nothing more than a "mere wish or plan" for a powder formulation and that the '793 patent contains no other disclosures relevant to developing a dry powder formulation of treprostinil that can be used for the claimed method of treating PH. (D.I. 406 at 22). I disagree.

The '793 patent describes the delivery of a therapeutically effective bolus dose of 15-90 µg of treprostinil by inhalation in 1-3 breaths without the expected negative side effects. (JTX 3 at Exs. 1 and 2, 17:4-24, 17:42-43, 18:4-6; Tr. at 832:19-833:6, 835:7-13, 836:17-21 (Clark)). The '793 patent demonstrates the efficacy of the claimed bolus dose by presenting data from the

administration of a liquid formulation of treprostinil in 1-3 breaths using a soft mist inhaler and an ultrasonic nebulizer. (JTX 3 at Exs. 1 and 2; Tr. at 832:19-833:6 (Clark)).

Liquidia claims that this information regarding liquid formulations in the '793 patent does not inform the development of powder formulations, relying on testimony from the '793 patent inventors Drs. Rubin and Seeger. (D.I. 406 at 21). But Dr. Rubin merely stated that a solution could not be used in a DPI; he never stated that information about an inhaled solution cannot be used to develop a powder formulation. (Tr. at 612:4-5 (Rubin)). Further, Dr. Seeger merely testified, "[B]ringing something down as a powder may or may not be simply identical to bringing something down with the fluid solution." (Tr. at 297:12-23 (Seeger)). These statements are not clear and convincing evidence that information regarding liquid formulations cannot inform the development of powder formulations.

Rather, UTC's expert Dr. Clark credibly testified that the "starting point for developing a powder formulation" is determining the dose and whether it is "safe to deliver it in a single bolus." (Tr. at 833:10-20 (Clark)). Although the '793 patent does not contain any examples of dry powder formulations or DPIs, the '793 patent discloses the bolus dose and demonstrates its efficacy. The patent further states that the claimed bolus dose of treprostinil can be delivered using a DPI with a powder formulation consisting of particles less than ten microns and preferably less than five microns. (JTX 3 at 7:22-26; Tr. at 834:9-15 (Clark)). Numerous DPIs were available by 2006 and the process for developing dry powder formulations was well known and involved routine techniques. (Tr. at 758:8-10,

761:19-23 (Gonda); Tr. at 835:24-836:3,837:19-838:1 (Clark); PTX 271 at 4; PTX 905).

Given the disclosures in the '793 patent and the state of the art, I find that a POSA would have understood that the inventors possessed a method of treating PH using a dry powder formulation of treprostinil with a DPI.[20] (*See* Tr. at 832:19-835:16 (Clark)); *Bos. Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011) ("Because the specification is viewed from the perspective of one of skill, in some circumstances, a patentee may rely on information that is 'well-known in the art' for purposes of meeting the written description requirement.").

I therefore find that Liquidia has failed to prove by clear and convincing evidence that claims 1, 4, 6, 7, and 8 of the '793 patent are invalid for lack of written description.

4. Enablement of Dry Powder Formulations and Dry Powder Inhaler

Liquidia argues that the '793 patent does not enable the claimed method of treating PH patients with a dry

---

[20] Liquidia also provides inventor testimony and evidence of UTC's agreement with MannKind to show that the inventors did not possess a dry powder formulation of treprostinil as of 2006. (*See* D.I. 406 at 22 & n.4). I have found, however, that the four corners of the specification reasonably convey possession of this limitation. Thus, this extrinsic evidence is irrelevant. *See Biogen Int'l GmbH v. Mylan Pharms. Inc.,* 28 F.4th 1194, 1202 (Fed. Cir. 2022) (Lourie, J., dissenting from the denial of the petition for rehearing en banc) ("Where the disclosure in a patent's specification plainly corresponds to what is claimed, extrinsic evidence should not be used to cast doubt on the meaning of what is disclosed."); *Ariad Pharms.,* 598 F.3d at 1352 ("[T]he written description requirement does not demand . . . an actual reduction to practice[.]").

powder treprostinil formulation and corresponding DPI. (D.I. 406 at 23-28).

The '793 patent does not provide any examples of treprostinil dry powder formulations, methods of manufacture of such powders, or DPI devices for the delivery of such formulations. (Tr. at 729:22-731:14 (Gonda); Tr. at 847:22-25 (Clark)). The processes involved in developing a dry powder formulation, however, were well known as of 2006. (Tr. at 837:19838:1, 838:15-841:3, 842:6-844:11, 845:17-846:14 (Clark); Tr. at 864:15-865:25, 867:8-870:15 (Smyth)).

Liquidia's expert Dr. Gonda testified that to develop a treprostinil dry powder formulation, a POSA would need to (1) identify a suitable form of treprostinil; (2) identify a suitable carrier that is safe and compatible with the API; and (3) identify a suitable DPI that can be used with the formulation to treat PH patients. (Tr. at 734:16-737:11 (Gonda)). Liquidia argues that a POSA would need to perform undue experimentation to perform these steps. (D.I. 406 at 24-25). Yet the experiments conducted by UTC's expert Dr. Smyth show otherwise.

With three weeks of testing, Dr. Smyth prepared treprostinil free acid and treprostinil diethanolamine dry powder formulations that delivered doses within the claimed 15-90 μg range. (Tr. at 863:6-864:14, 870:9-15, 876:18-879:8 (Smyth); PTX 1344; PTX 1345). Dr. Smyth used well-known and routine techniques for each step of his powder development process. (Tr. at 864:15-865:25, 867:8-876:17 (Smyth)). At a high level, Dr. Smyth's experiments involved jet milling the API several times, blending the formulations with lactose, adding the formulations to capsules, and testing the capsules using a DPI device and machine called a Next

Generation Impactor, intended to mimic patient inhalation. (Tr. at 864:23-865:3 (Smyth)).

Based on this testing, I find that Liquidia has failed to prove by clear and convincing evidence that a POSA would need to perform undue experimentation to develop a treprostinil dry powder formulation. *See Bristol-Myers Squibb Co. v. Aurobindo Pharma USA Inc.*, 477 F. Supp. 3d 306,352-53 (D. Del. 2020) (finding that defendants failed to prove lack of enablement where plaintiff's expert could successfully practice the claims), *aff'd sub nom. Bristol-Myers Squibb Co. v. Sigmapharm Lab'ys, LLC*, 858 F. App'x 359 (Fed. Cir. 2021).

First, Liquidia has failed to prove that a POSA would need to perform undue experimentation to identify a suitable form of treprostinil. The patent identifies the API to be used in the claimed invention: "treprostinil or a pharmaceutically acceptable salt thereof." (JTX 3 at claim 1; *see also id* at 6:41-7:6 (defining what constitutes a "pharmaceutically acceptable salt" of treprostinil)). Methods for determining suitable forms, including salt forms, of a particular API were well known and routine for several decades prior to 2006. (Tr. at 761:4-10 (Gonda); Tr. at 838:19-839:4,8414-21 (Clark)).

Dr. Smyth tested three forms of treprostinil: treprostinil free acid, treprostinil diethanolamine salt, and treprostinil sodium. Dr. Smyth was unable to develop a dry powder formulation of treprostinil sodium because it was too hygroscopic. (Tr. at 737:24-740:13 (Gonda); Tr. at 880:19-881:8 (Smyth)). Dr. Smyth attributed this to the lack of humidity control in his lab. (Tr. at 882:9-883:23 (Smyth)). I do not think Dr. Smyth's failure in developing a dry powder formulation of treprostinil sodium shows by clear and convincing evidence that a POSA would require undue experimentation to identify

a suitable form of treprostinil. Dr. Smyth used routine techniques to determine that treprostinil sodium would not work. Further, Dr. Gonda testified that a POSA in 2006 would have a laboratory with temperature and humidity control. (Tr. at 762:4-14 (Gonda)).

Liquidia also faults Dr. Smyth's experiments with treprostinil free acid. Treprostinil free acid is not stable at room temperature and has the tendency to form dimers. (DTX 674 at 4; Tr. at 741:20-744:4 (Gonda)). Liquidia argues that despite this, Dr. Smyth did not test the stability of his treprostinil free acid powder formulation. (D.I. 406 at 27). Dr Smyth's failure to conduct additional testing is not clear and convincing evidence that undue experimentation would be required to select a suitable form of treprostinil. Dr. Gonda testified that "stability testing" was known and routine by 2006. (Tr. at 770:15-16 (Gonda)). Further, Liquidia did not perform extensive stability tests in selecting the API for LIQ861. (Tr. at 275:10-24 (Maynor)).

Second, Liquidia has failed to prove that a POSA would require undue experimentation to identify a suitable carrier. Although the '793 patent does not disclose any suitable carriers, lactose was the only FDA-approved carrier for dry powder formulations as of 2006. (PTX 905 at 13; Tr. at 763:14-21 (Gonda); Tr. at 844:12-15 (Clark); Tr. at 866:1-4 (Smyth)). For this reason, Dr. Smyth selected lactose as the carrier for his dry powder formulations. (Tr. at 866:1-4 (Smyth)).

Dr. Gonda testified that "a POSA would have been reluctant to use lactose" as a carrier with treprostinil diethanolamine because lactose reacts with amines by the Maillard reaction. (Tr. at 754:1-11 (Gonda); *see also*

DTX 481).[21] According to UTC's expert Dr. Clark, however, the Maillard reaction would not deter a POSA from attempting to formulate an amine drug with lactose unless the POSA witnessed an adverse reaction. (Tr. at 844:16-845:2 (Clark)). Dr. Clark reasoned that in 2006, the Physician's Desk Reference—which generally only describes approved drugs—described 72 examples of amine drugs formulated with lactose. (Tr. at 844:12-23 (Clark); Tr. at 866:5-867:7 (Smyth); PTX 47 at 2). Further, a POSA would have understood how to monitor any Maillard reaction between treprostinil diethanolamine and lactose. (Tr. at 844:16-845:2 (Clark); PTX 47 at 2; DTX 481 at 5). There is no evidence that Dr. Smyth noticed any Maillard reaction with treprostinil diethanolamine. (*See* Tr. at 867:22-870:15 (Smyth)). I am therefore not convinced that a POSA would require undue experimentation to select an appropriate carrier.

Third, Liquidia has not proven that identifying a suitable DPI for PH patients would require undue experimentation. A 2005 publication by Meyer et al. discloses that PH patients were able to obtain maximum inspiratory efforts of 5.2 kPa in females and 6.8 kPa in males, which is enough to use a DPI. (PTX 1980 at 1; Tr. at 851:20-852:1, 852:14-854:20 (Clark)). Dr. Smyth's analytical testing involved the use of a Next Generation Impactor simulating a single breath at 4.0 kPa and 4.0L through a Plastiape RS01 low resistance inhaler (which was available as of 2006). (Tr. at 869:22-870:8

[21] There is no amine in the treprostinil molecule itself, so a POSA would have no concern about the Maillard reaction with respect to combining treprostinil free acid and lactose. (Tr. at 767:23-768:8 (Gonda)).

(Smyth); Tr. at 845:17-846:8 (Clark); PTX 905 at 7).[22] Dr. Smyth's testing resulted in an average emitted dose of 53.54 µg for treprostinil free acid and 52.60 µg for treprostinil diethanolamine, falling well within the claimed range of 15-90 µg. (PTX 1344 at 2; PTX 1345 at 2). Dr. Smyth's testing demonstrated that PH patients could effectively inhale his dry powder formulations using a DPI.

I find that a POSA reading the '793 patent would be able to develop a dry powder formulation of treprostinil and a corresponding DPI for treatment of PH with routine experimentation. Notably, Liquidia and its experts did not perform any experiments attempting to make dry powder formulations. Liquidia instead tries to discredit Dr. Smyth's testing. But, for the reasons discussed above, these efforts do not amount to clear and convincing evidence that a POSA would require undue experimentation. That Dr. Smyth would not administer his dry powder formulations to PH patients without conducting more studies makes no difference. (*See* D.I. 406 at 28). Of course, there is no

[22] Liquidia challenges Dr. Smyth's testing on the basis that he "assumed large inhaled volumes and flow rates." (D.I. 406 at 28). Dr. Smyth did not explicitly set forth his assumed inspiratory effort (4.0 kPa) and inhaled volume (4.0 L) in his testimony, but these values were set forth on a demonstrative exhibit. (DDX 5.4). Liquidia argues that these values were too high as a 2021 article by Faria-Urbina et al. reported that PAH patients have a maximum inspiratory pressure of 2.6 ± 1.2 kPa and inhale a total volume of 1.4 ± 0.03 L. (DTX 468 at 4 (Table 2); Tr. at 751:14754:13 (Gonda); Tr. at 854:16-20 (Clark)). I nevertheless find Dr. Smyth's testing to be credible. The assumed inspiratory pressure of 4.0 kPa is consistent with the maximum inspiratory pressure reported in Meyer (5.2 kPa in females, 6.8 kPa in males). Meyer was available to a POSA as of 2006, unlike the 2021 Faria-Urbina publication.

expectation that Dr. Smyth test his formulations on actual patients for purposes of patent litigation.

Liquidia also argues that UTC is improperly "attempting to use a POSA's knowledge as an entire substitute for a deficient specification." (*Id.* at 26 (citing *Trs. of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1364 (Fed. Cir. 2018); *Auto. Techs. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1283 (Fed. Cir. 2007))). I do not think that is the case. The '793 patent teaches a POSA that a bolus dose of 15-90 µg of treprostinil delivered by inhalation in 1-3 breaths provides therapeutic efficacy without the expected negative side effects. (JTX 3 at Exs. 1 and 2, 17:4-24, 17:42-43, 18:4-6; Tr. at 832:19-833:6, 835:7-13, 836:17-21 (Clark); *see also* JTX 3 at 2:60-62 ("Currently, there is no treatment for pulmonary hypertension that can be administered using a compact inhalation device such as a metered dose inhaler.")). UTC's experts Dr. Smyth and Dr. Clark supplemented these disclosures by showing that a POSA at the time of the invention would have been able to use well-known and routine techniques to make the claimed dry powder formulations. *See AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003) ("[T]he artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art.").

I therefore find that Liquidia has failed to prove by clear and convincing evidence that claims 1, 4, 6, 7, and 8 of the '793 patent are invalid for lack of enablement.

VI. CONCLUSION

UTC failed to prove by a preponderance of the evidence that Liquidia will infringe claim 8 of the '066

patent. Liquidia proved by clear and convincing evidence that claims 1, 2, 3, 6, and 9 of the '066 patent are invalid. UTC proved by a preponderance of the evidence that Liquidia will induce infringement of claims 1, 4, 6, 7, and 8 of the '793 patent.

The parties shall submit a final judgment consistent with this memorandum opinion within one week.

APPENDIX D

NOTE: This order is nonprecedential.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2022-2217, 2023-1021

UNITED THERAPEUTICS CORPORATION,

Plaintiff-Cross-Appellant

v.

LIQUIDIA TECHNOLOGIES, INC.,

Defendant-Appellant

Appeals from the United States District Court for the District of Delaware in No. 1:20-cv-00755-RGA-JLH, Judge Richard G. Andrews.

ON PETITIONS FOR PANEL REHEARING
AND REHEARING EN BANC

Before MOORE, Chief Judge, LOURIE, DYK, PROST, REYNA, TARANTO, CHEN, HUGHES, STOLL, and CUNNINGHAM, *Circuit Judges*.[1]

PER CURIAM.

---

[1] Circuit Judge Newman and Circuit Judge Stark did not participate.

ORDER

On August 23, 2023, Liquidia Technologies, Inc. and United Therapeutics Corporation separately filed combined petitions for panel rehearing and rehearing en banc. The petitions were referred to the panel that heard the appeal, and thereafter the petitions were referred to the circuit judges who are in regular active service.

Upon consideration thereof,

IT IS ORDERED THAT:

The petitions for panel rehearing are denied.

The petitions for rehearing en banc are denied.

The mandate of the court will issue October 3, 2023.

FOR THE COURT

September 26, 2023
Date

[SEAL]
/s/ Jarrett B. Perlow
Jarrett B. Perlow
Clerk of Court

APPENDIX E

Entered: July 19, 2022

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LIQUIDIA TECHNOLOGIES, INC.,

Petitioner,

v.

UNITED THERAPEUTICS CORPORATION,

Patent Owner.

IPR2021-00406
Patent 10,716,793 B2

Before ERICA A. FRANKLIN, CHRISTOPHER M. KAISER, and DAVID COTTA, *Administrative Patent Judges.*

KAISER, *Administrative Patent Judge*.

JUDGMENT

Final Written Decision

Determining All Challenged Claims Unpatentable

35 U.S.C. § 318(a)

INTRODUCTION

A. Background

Liquidia Technologies, Inc. ("Petitioner") filed a Petition (Paper 2, "Pet.") requesting an *inter partes* review of claims 1–8 of U.S. Patent No. 10,716,793 B2 (Ex. 1001, "the '793 patent"). United Therapeutics Corporation ("Patent Owner") filed a Preliminary Response. Paper 13 ("Prelim. Resp.").

On August 11, 2021, we instituted *inter partes* review of claims 1–8 of the '793 patent on all grounds set forth in the Petition. Paper 18 ("Inst. Dec."). After institution of trial, Patent Owner filed a Response (Paper 29, "PO Resp."), Petitioner filed a Reply (Paper 44), and Patent Owner filed a Sur-Reply (Paper 55). In addition, both parties filed Motions to Exclude Evidence (Papers 65 and 66), Oppositions to their respective opponents' Motions to Exclude (Papers 68 and 69), and Replies in support of their own Motions to Exclude (Papers 71 and 72). At the request of both parties, we held an oral hearing, the transcript of which has been entered into the record. Paper 77 ("Tr.").

We have jurisdiction under 35 U.S.C. § 6. This is a Final Written Decision under 35 U.S.C. § 318(a) as to the patentability of the challenged claims of the '793 patent. For the reasons discussed below, we determine Petitioner has established by a preponderance of the evidence that each of claims 1–8 of the '793 patent is unpatentable.

B. Related Matters

The parties identify *United Therapeutics Corporation v. Liquidia Technologies, Inc.*, 1:20-cv-00755-

RGA (D. Del.) ("the District Court proceeding"), as a related matter. Pet. 1; Paper 3, 1.

C. The Asserted Grounds of Unpatentability

Petitioner contends that claims 1–8 of the '793 patent are unpatentable based on the following grounds (Pet. 30–68):[1]

Claim(s) Challenged	35 U.S.C. §[2]	Reference(s)/Basis
1–8	103(a)	'212 patent,[3] Voswinckel JESC,[4] Voswinckel JAHA[5]
1–8	103(a)	'212 patent, Voswinckel JESC
1	102(a)	Ghofrani[6]

[1] Petitioner also relies on declarations from Nicholas Hill, M.D., and Igor Gonda, Ph.D. Exs. 1002, 1004, 1106, 1107.

[2] The '793 patent claims a priority date of May 15, 2006, and Petitioner "assumes the relevant priority date . . . is May 15, 2006." Pet. 12; Ex. 1001, code (60). Accordingly, patentability is governed by the versions of 35 U.S.C. §§ 102 and 103 preceding the amendments in the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011).

[3] US 6,521,212 B1, issued Feb. 18, 2003 (Ex. 1006) (alleged to be prior art under 35 U.S.C. §§ 102(a), (b), (e)).

[4] Voswinckel, R., et al., *Inhaled treprostinil is a potent pulmonary vasodilator in severe pulmonary hypertension*, 25 EUROPEAN HEART J. 22 (2004) (Ex. 1007) (alleged to be prior art under 35 U.S.C. § 102(b)).

[5] Robert Voswinckel, et al., *Inhaled Treprostinil Sodium (TRE) For the Treatment of Pulmonary Hypertension*, in Abstracts from the 2004 Scientific Sessions of the American Heart Association, 110 CIRCULATION III-295 (Oct. 26, 2004) (Ex. 1008) (alleged to be prior art under 35 U.S.C. § 102(b)).

1, 3, 8	103(a)	Voswinckel JAHA, Ghofrani
1, 3	102(a)	Voswinckel 2006[7]

Claim(s) Challenged	**35 U.S.C. §[2]**	**Reference(s)/Basis**
2, 4–8	103(a)	Voswinckel 2006, '212 patent

D. The '793 Patent

The '793 patent, titled "Treprostinil Administration by Inhalation," issued on July 21, 2020. Ex. 1001, codes (45), (54). The patent "relates to methods and kits for therapeutic treatment and, more particularly, to therapeutic methods involving administering treprostinil using a metered dose inhaler and related kits." *Id.* at 1:20–23.

Treprostinil "is a prostacyclin analogue" that may be used to treat pulmonary hypertension. *Id.* at 5:37–41. According to the '793 patent, it was previously known to administer treprostinil by intravenous, subcutaneous, or inhalation routes to treat any of several conditions, including pulmonary hypertension. *Id.* at 5:42–58.

---

[6] Hossein Ardeschir Ghofrani, et al., *Neue Therapieoptionen in der Behandlung der pulmonalarteriellen Hypertonie*, 30 HERZ 296–302 (June 2005) (Ex. 1010) (alleged to be prior art under 35 U.S.C. § 102(a)). We rely on the English translation that follows the German original article as part of Ex. 1010.

[7] Robert Voswinckel, et al., *Inhaled Treprostinil for Treatment of Chronic Pulmonary Arterial Hypertension*, 144 ANNALS OF INTERNAL MEDICINE 149–50 (January 2006) (Ex. 1009) (alleged to be prior art under 35 U.S.C. § 102(a)).

The '793 patent relates to the administration of treprostinil in high concentrations over a short inhalation time. *Id.* at 16:61–63, 17:44–46. This method of administration is described as reducing pulmonary vascular resistance and pulmonary artery pressure, as well as increasing cardiac output. *Id.* at 16:32–42, Fig. 10.

E. Illustrative Claim

Claims 1–8 of the '793 patent are challenged. Claim 1 is independent and illustrative; it recites:

> 1. A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

Ex. 1001, 18:23–31.

ANALYSIS

A. Claim Construction

In an *inter partes* review, we construe a claim in an unexpired patent "in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." 37 C.F.R. § 42.100(b) (2020). "[T]he ordinary and customary meaning of a claim term 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." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). "Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id.*

Neither party presents any terms for construction. Pet. 12–13 ("Petitioner does not believe construction of any claim term is required"); PO Resp. 7 (not proposing construction of any terms). Accordingly, we determine that no express construction of any claim term is necessary in order to decide whether to institute trial. *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (citing *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy.")).

B. Asserted Obviousness over '212 Patent, Voswinckel JESC, and Voswinckel JAHA

Petitioner argues that claims 1–8 would have been obvious over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA. Pet. 30–46. Patent Owner argues that Petitioner fails to show that Voswinckel JESC and Voswinckel JAHA are prior art to the '793 patent. PO Resp. 11–18. Patent Owner also argues that Petitioner fails to show that this combination of references teaches or suggest all the limitations of any of the challenged claims. PO Resp. 18–22, 38–40. In addition, Patent Owner also argues that Petitioner fails to show that a person of ordinary skill in the art would have had a reason to

combine the teachings of these references. *Id.* at 23–38.

1. '212 Patent

The '212 patent teaches "[a] method of delivering benzindene prostaglandins to a patient by inhalation." Ex. 1006, code (57). In particular, the '212 patent teaches the use of "[a] benzindene prostaglandin known as UT-15," which "has unexpectedly superior results when administered by inhalation compared to parenterally administered UT-15 in sheep with induced pulmonary hypertension." *Id.* There is evidence in the present record that "UT-15" was also known as "Remodulin" or "treprostinil sodium." Ex. 1035, 582. According to the '212 patent, the UT-15 may be delivered either as droplets formed "from a solution or liquid containing the active ingredient(s)" via a nebulizer, or as a solid-phase powder via an inhaler. Ex. 1006, 5:30–41.

According to the '212 patent, this method may be used to "treat[] pulmonary hypertension in a mammal." *Id.* at 14:9–12. Moreover, the '212 patent teaches "medical use" of its method in a "human." *Id.* at 7:4–5. The necessary dose to achieve "a particular therapeutic purpose will, of course, depend upon the specific circumstances of the patient being treated and the magnitude of the effect desired by the patient's doctor. Titration to effect may be used to determine proper dosage." *Id.* at 6:66–7:3. "[A]erosolized UT-15 has a greater potency as compared to intravascularly administered UT-15," so the '212 patent teaches delivering "only a fraction (10–50%) of the dosage delivered intravascularly" when using its inhalation delivery method. *Id.* at 8:8–12. Even at "high doses," however, the '212 patent teaches a lack

of "significant non-lung effects, i.e., heart rate, cardiac output." *Id.* at 10:51–54.

2. Voswinckel JESC

Voswinckel JESC discusses a study to investigate "the acute hemodynamic response to inhaled treprostinil." Ex. 1007, 7. Of the 29 patients in the study, eight were administered a placebo, groups of six patients each were administered 16, 32, and 48 µg/mL solutions of treprostinil, and three patients were administered a solution containing 64 µg/mL of treprostinil. *Id.* Each administration used an "OptiNeb ultrasound nebulizer, [made by] Nebu-Tec, Germany" for six minutes. *Id.* For each patient, various measurements were taken before administration of the treprostinil and at 0, 15, 30, 60, 90, 120, 150, and 180 minutes after administration. *Id.* According to Voswinckel JESC, "[t]reprostinil inhalation results in a significant long-lasting pulmonary vasodilatation," and, "at a concentration of 16 µg/mL, near maximal pulmonary vasodilatation is achieved without adverse effects." *Id.*

3. Voswinckel JAHA

Voswinckel JAHA discusses a study of 17 patients with "severe pulmonary hypertension" who received treprostinil inhalations. Ex. 1008, 3. These inhalations each involved "3 single breaths" using a "pulsed OptiNeb® ultrasound nebulizer" and a "600 µg/mL" treprostinil solution. *Id.* In addition, "[t]wo patients with idiopathic PAH received compassionate treatment with 4 inhalations of TRE per day after the acute test" and were "treated for more than 3 months." *Id.* According to Voswinckel JAHA, "inhalation resulted in a sustained, highly pulmonary selective vasodilatation over 120 minutes," showing

"strong pulmonary selective vasodilatory efficacy with a long duration of effect following single acute dosing," and "[t]olerability is excellent even at high drug concentrations and short inhalation times (3 breaths)." *Id.*

4. Prior-Art Status of Voswinckel JESC and Voswinckel JAHA

In arguing that claims 1–8 would have been obvious, Petitioner relies on Voswinckel JESC and Voswinckel JAHA, but Patent Owner argues that Petitioner fails to show sufficiently that either of these references qualifies as a "printed publication." PO Resp. 11–18.

Only "prior art consisting of patents or printed publications" may form "the basis of" an *inter partes* review. 35 U.S.C. § 311(b). Neither Voswinckel JESC nor Voswinckel JAHA is a patent, so Petitioner may not rely on these references unless they are "printed publications." *Id.* Public accessibility is the "touchstone in determining whether a reference constitutes a printed publication," and a reference is considered publicly accessible only if it was "disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it." *Kyocera Wireless Corp. v. Int'l Trade Comm'n*, 545 F.3d 1340, 1350 (Fed. Cir. 2008) (quoting *SRI Int'l, Inc. v. Internet Sec. Sys. Inc.*, 511 F.3d 1186, 1194 (Fed. Cir. 2008); *In re Hall*, 781 F.2d 897, 898–99 (Fed. Cir. 1986)).

Patent Owner argues that, because Petitioner relies on Voswinckel JESC and Voswinckel JAHA having been "stored in libraries, public accessibility requires that the reference be both available at the

library and sufficiently indexed or catalogued by the priority date." PO Resp. 12 (citing *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1348 (Fed. Cir. 2016); *In re Klopfenstein*, 380 F.3d 1345, 1349 (Fed. Cir. 2004)). According to Patent Owner, Petitioner fails to show sufficiently either of these requirements. *Id.* at 12–18.

But Petitioner does not rely solely on availability in libraries to show the prior-art status of Voswinckel JESC and Voswinckel JAHA. Instead, Petitioner also argues that "Voswinckel JESC is an abstract presented at the European Society of Cardiology (JESC) Congress," that Voswinckel JAHA "was publicly presented at the 2004 Scientific Sessions of the American Heart Association," and that both references were cited in other documents dating from before the priority date of the '793 patent whose public accessibility is not at issue. Pet. 22; Reply 3–4, 6–8.

Patent Owner objects that Petitioner's public-presentation and citation-in-other-references arguments are untimely because they should have been, but were not, presented in the Petition. Sur-Reply 2–3. We disagree. First, the argument that Voswinckel JESC was presented publicly appears in the Petition. Pet. 22. Second, although other of Petitioner's arguments appear for the first time in the Reply, they are not untimely. Reply 3–4, 6–8.

Petitioner is permitted a "limited opportunit[y]" to present new evidence in or with its Reply, as long as that new evidence is "responsive to the prior briefing" and does not constitute "changing theories after filing [the] petition." *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018- 01039, Paper 29, at 14–15 (PTAB Dec. 20, 2019) (precedential). Here, both of the argu-

ments that Patent Owner alleges are new—the argument that Voswinckel JESC and Voswinckel JAHA were presented publicly and the argument that these references were cited in other publicly available references—respond to Patent Owner's argument in the Patent Owner Response that Voswinckel JESC and Voswinckel JAHA were not publicly accessible. PO Resp. 11–18. The argument that Voswinckel JESC was publicly presented is not a change in theory from the Petition, because Petitioner presented this argument in the Petition. Pet. 22. As to both Voswinckel JESC and Voswinckel JAHA, Petitioner's Reply evidence showing citation to the references in other publicly accessible documents is merely additional evidence supporting Petitioner's original theory that a person of ordinary skill in the art could have located the references. Accordingly, we find that the following arguments made by Petitioner are not untimely: (1) that Voswinckel JESC was presented publicly, (2) that Voswinckel JESC was referenced in a publicly accessible document, and (3) that Voswinckel JAHA was referenced in a publicly accessible document.

Given the evidence supporting Petitioner's timely arguments, we are persuaded that Petitioner has shown by a preponderance of the evidence that Voswinckel JESC and Voswinckel JAHA were publicly accessible. "[T]he presence of a 'research aid' can . . . establish public accessibility" of a reference if that research aid "provide[s] a skilled artisan with a sufficiently definite roadmap leading to" the reference by "provid[ing] enough details [to] determine that an interested party is reasonably certain to arrive at the destination: the potentially invalidating reference." *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1350 (Fed. Cir. 2016).

Here, Petitioner directs us to research aids for finding both Voswinckel JESC and Voswinckel JAHA: a "June 2005 Ghofrani article in the journal *Herz*" for the former, and "a March 2005 article authored by Roxana Sulica et al. in the *Expert Review of Cardiovascular Therapy*" for the latter. Reply 3, 7 (citing Ex. 1010, 298, 301; Ex. 1104, 359). The Ghofrani article cites Voswinckel JESC as providing a solution to patients experiencing "pain at the injection site" by replacing injected treprostinil for "pulmonary arterial hypertension" with "*inhaled* treprostinil." Ex. 1010, 298 (citing reference 6), 301 (defining reference 6 as Voswinckel JESC). The Ghofrani article also discusses the study reported in Voswinckel JESC, summarizing both the "major reduction in pulmonary selective pressure and resistance" and the lack of "adverse effects" described in Voswinckel JESC. *Id.* The Sulica article cites to Voswinckel JAHA, explaining that the reference reports that "inhaled treprostinil demonstrated substantial pulmonary vasodilatory efficacy in acute administration, as well as symptomatic and functional benefit in chronic use in a small number of PAH patients." Ex. 1104, 351, 359. Thus, both the Ghofrani article and the Sulica article provide roadmaps directing a person of ordinary skill in the art looking for successful studies discussing the use of inhaled treprostinil in pulmonary arterial hypertension straight to Voswinckel JESC or Voswinckel JAHA. Because these articles provide these roadmaps, they are "research aid[s]" that "establish [the] public accessibility" of Voswinckel JESC and Voswinckel JAHA. *Blue Calypso*, 815 F.3d at 1350.

5. Analysis

Petitioner argues that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests the subject matter of claims 1–8 and that a person of ordinary skill in the art would have had a reason to combine the teachings of these references with a reasonable expectation of success. Pet. 30–46. Patent Owner argues that this combination of references fails to teach or suggest delivering a dose of treprostinil within the dose range of the challenged claims in a single dosing event of one to three breaths. Prelim. Resp. 42–55.

a. Claim 1

(1) "A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof"

Claim 1 recites "[a] method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof." Ex. 1001, 18:23–27. Petitioner argues that the '212 patent, Voswinckel JESC, and Voswinckel JAHA each teach or suggest this limitation. Pet. 35–37. Patent Owner does not dispute this argument. PO Resp. 10–40.

The '212 patent teaches treating pulmonary hypertension via inhalation of a benzindene prostaglandin called UT-15, which was also known as "treprostinil

sodium." Ex. 1006, code (57) (identifying "benzindene prostaglandin" as "UT-15"), 2:66–3:5 ("This invention relates to . . . a method of treating pulmonary hypertension by administering an effective amount of a benzindene prostaglandin to a mammal in need thereof by inhalation."); Ex. 1035, 582 ("UT-15" also known as "treprostinil sodium"). Voswinckel JAHA teaches treating "patients with severe pulmonary hypertension" with "Inhaled Treprostinil Sodium (TRE)" with "3 single breaths" of "TRE solution 600 µg/ml," resulting in "strong pulmonary selective vasodilatory efficacy with a long duration of effect following single acute dosing." Ex. 1008, 3. Voswinckel JESC describes "the acute hemodynamic response to inhaled treprostinil" following the administration to patients of nebulized treprostinil solution in concentrations of 16, 32, 48, and 64 µg/ml for six minutes, resulting in "significant long- lasting pulmonary vasodilatation" without "adverse effects." Ex. 1007, 7.

Accordingly, Petitioner has shown by a preponderance of the evidence that the '212 patent, Voswinckel JESC, and Voswinckel JAHA each teach or suggest this portion of claim 1.

(2) "With an inhalation device"

Next, claim 1 recites "with an inhalation device." Ex. 1001, 18:27–28. Petitioner argues that the '212 patent, Voswinckel JESC, and Voswinckel JAHA each teach or suggest this limitation. Pet. 37. Patent Owner does not dispute this argument. PO Resp. 10–40. The '212 patent teaches the use in its inhalation method of "a nebulizer, inhaler, atomizer or aerosolizer" to "form[] droplets from a solution or liquid containing the active ingredient(s)." Ex. 1006, 5:30–32. Both Voswinckel JESC and Voswinckel JAHA

teach the use of a "nebulizer" in their inhalation methods. Ex. 1007, 7 ("OptiNeb ultrasound nebulizer"); Ex. 1008, 3 ("the pulsed OptiNeb® ultrasound nebulizer"). Dr. Hill testifies that a person of ordinary skill in the art would have understood "that nebulizers and inhalers are inhalation devices." Ex. 1002 ¶ 94. Accordingly, Petitioner has shown by a preponderance of the evidence that the '212 patent, Voswinckel JESC, and Voswinckel JAHA each teach or suggest this limitation of claim 1.

> *(3) "Wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof"*

Claim 1 recites "wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof." Ex. 1001, 18:28–30. Petitioner argues that the combination of the '212 patent and Voswinckel JESC teaches or suggests this limitation. Pet. 37–40. Patent Owner disagrees. PO Resp. 18–38.

Petitioner calculates the dose that the prior art teaches delivering by inhalation in three separate ways: (1) relying on Voswinckel JESC's solution concentrations and solution volumes taught by Ex. 1037, (2) relying on Voswinckel JESC's solution concentrations and solution volumes normally delivered according to the testimony of Petitioner's declarants, and (3) relying on the '212 patent's conversion from an intravascular treprostinil dose to an equivalent inhaled dose. Pet. 22–24, 38–39. According to Petitioner, each of these three calculation methods results in a teaching of a therapeutically effective

single event dose comprising from 15 micrograms to 90 micrograms of treprostinil. *Id.*

We agree with Patent Owner that Petitioner's first and third calculation methods do not demonstrate that the prior art taught or suggested a therapeutically effective single event dose comprising from 15 micrograms to 90 micrograms of treprostinil, and we do not discuss these calculations any further. The preponderance of the evidence, however, supports Petitioner's argument that its second calculation demonstrates that the prior art taught or suggested a therapeutically effective single event dose comprising from 15 micrograms to 90 micrograms of treprostinil.

Voswinckel JESC teaches that "patients inhaled solvent solution (placebo) (n=8) or treprostinil for 6 min (OptiNeb ultrasound nebulizer, Nebu-tec, Germany) in concentrations of 16, 32, 48, and 64 µg/ml (n=6, 6, 6, and 3 patients)." Ex. 1007, 7. Although this teaching shows administration to patients of inhaled solutions with particular concentrations of treprostinil, it does not disclose the amount of solution administered, which is necessary in order to calculate the amount of treprostinil administered. *Id.* Petitioner directs us to the testimony of its declarants, Dr. Nicholas Hill and Dr. Igor Gonda, to understand how a person of ordinary skill in the art would have interpreted Voswinckel JESC's disclosure. Pet. 23 (citing Ex. 1002 ¶ 65; Ex. 1004 ¶ 56). Dr. Gonda testifies that "in May 2006 . . . nebulizers conventionally deliver[ed] between 1 and 5 mL" of solution. Ex. 1004 ¶ 56. Relying on Dr. Gonda's testimony as well as his own experience, Dr. Hill testifies that a person of ordinary skill in the art in 2006 would have understood that "nebulizers . . . nebulize (i.e. aerosolize liquid) at least" 1 mL of

solution. Ex. 1002 ¶ 65. Multiplying Voswinckel JESC's 16, 32, 48, or 64 micrograms of treprostinil per milliliter of solution by the 1 to 5 milliliters of solution in the testimony of Drs. Hill and Gonda, a person of ordinary skill in the art would have interpreted Voswinckel JESC as teaching the delivery of 16–80, 32–160, 48–240, or 64–320 micrograms of treprostinil. Each of those four dose ranges has at least one endpoint that falls within the 15–90 microgram claimed range.

Patent Owner argues that this evidence is insufficient to show that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests a therapeutically effective single event dose comprising from 15 micrograms to 90 micrograms of treprostinil. Specifically, Patent Owner argues that the volume of solution that Drs. Hill and Gonda testify was typically used in nebulizers is "the fill volume," or the amount of solution loaded into a nebulizer to be nebulized, which cannot be used with the concentrations in Voswinckel JESC to arrive at the amount of treprostinil actually delivered to a patient. PO Resp. 30–31. This is because "there is no guarantee that the entire fill volume would be completely nebulized in" the time period over which Voswinckel JESC teaches delivering its dose of treprostinil. *Id.* at 30. In addition, Patent Owner argues that there were other factors that might have caused less than all the solution nebulized by a nebulizer to be actually delivered to the patient, none of which Petitioner accounts for. *Id.* at 31–32.

Petitioner "presented evidence that nebulizers at the time typically involved fill volumes of 1-5mL." Reply 10–11. To the extent that something less than the entire fill volume was delivered to the patient,

either because it was not nebulized or because other factors resulted in the nebulized solution not reaching the mouthpiece, the preponderance of the evidence still supports the actual delivered solution volume being at least one milliliter. Dr. Hill testifies that the "at least 1 mL" of solution he discusses is the volume that "nebulizers at the time were known to nebulize," not the amount of liquid loaded into the nebulizer. Ex. 1002 ¶ 65. Patent Owner's declarant, Dr. Aaron Waxman, testifies that standard nebulizers had fill volumes of "3 to 5 [milliliters]" and that he had never administered a dose as low as one milliliter to a patient. Ex. 1108, 153:1–22; 156:12–16.

Thus, Voswinckel JESC teaches delivering solution with a treprostinil concentration of 16, 32, 48, or 64 micrograms per milliliter, and the preponderance of the evidence supports a finding that a person of ordinary skill in the art would have understood the volume of solution delivered in Voswinckel JESC to be at least one milliliter. Accordingly, Petitioner has shown by a preponderance of the evidence that Voswinckel JESC teaches or suggests a therapeutically effective single event dose comprising from 15 micrograms to 90 micrograms of treprostinil.

(4) "Delivered in 1 to 3 breaths"

Claim 1 recites "delivered in 1 to 3 breaths." Ex. 1001, 18:31. Petitioner argues that Voswinckel JAHA teaches or suggests this limitation. Pet. 40–41. Patent Owner does not dispute this teaching of Voswinckel JAHA. PO Resp. 10–40.

Voswinckel JAHA teaches delivering to patients "a TRE inhalation by use of the pulsed OptiNeb® ultrasound nebulizer (3 single breaths, TRE solution 600 µg/ml)." Ex. 1008, 3. It also reports that

"[t]olerability is excellent even at high drug concentrations and short inhalation times (3 breaths)." *Id.* Accordingly, Petitioner has shown by a preponderance of the evidence that Voswinckel JAHA teaches or suggests this limitation of claim 1.

b. Reason to Combine with a Reasonable Expectation of Success

As discussed above, Petitioner has shown sufficiently on the present record that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests every limitation of claim 1. This alone is not sufficient to show that the challenged claims would have been obvious; Petitioner also must show that a person of ordinary skill would have had a reason to combine the teachings of the references and would have had a reasonable expectation of success in doing so.

Petitioner argues that a person of ordinary skill in the art would have had a reason to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA. Pet. 30–34. Patent Owner argues that a person of ordinary skill in the art would have had "serious concerns about side effects" that would have persuaded them not to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA. PO Resp. 37–38.

The '212 patent teaches the use of inhaled treprostinil sodium for the treatment of pulmonary hypertension at doses between 10 and 50 percent of the doses needed for intravascular delivery. Ex. 1006, code (57), 6:1–2, 8:8–12. According to the '212 patent, the inhaled treprostinil sodium is used in sheep, which are a model for pulmonary hypertension in humans. *Id.* at 9:14–27. Dr. Hill testifies that, based

on these teachings, a person of ordinary skill in the art would have looked for further information regarding "experimentation [with] inhaled treprostinil in humans." Ex. 1002 ¶ 78. On the present record, such information can be found in Voswinckel JESC, which reports on a study in which humans with pulmonary hypertension inhaled treprostinil and experienced "significant long-lasting pulmonary vasodilatation . . . without adverse effects." Ex. 1007, 7.

Dr. Hill testifies that, based on the teachings of these references a person of ordinary skill would reasonably have expected that treprostinil could safely and effectively treat pulmonary hypertension in humans. Ex. 1002 ¶ 79. Dr. Hill also testifies that a person of ordinary skill in the art "would have been motivated to further decrease the 6 minute administration time in Voswinckel JESC." Ex. 1002 ¶ 80. Specifically, Dr. Hill testifies that patients often did not adhere to "inhalation therapy for respiratory diseases," that "[p]oor adherence to medication was known to correlate with worse outcomes," and that "reducing administration time or the number of breaths required for therapy [was known to] improve adherence rates." *Id.* (citing Ex. 1002 ¶¶ 36–37; Ex. 1030, 63; Ex. 1032, 179–80; Ex. 1077, 4). Voswinckel JAHA teaches administering treprostinil in three breaths using a high concentration of treprostinil in the aerosolized solution. Ex. 1008, 3. Accordingly, Dr. Hill testifies that a person of ordinary skill in the art would have looked to Voswinckel JAHA to improve patient adherence to the treatment suggested by the combination of the '212 patent and Voswinckel JESC, providing a reason to combine its teachings with those of the other two references. Ex. 1002 ¶¶ 80–82.

Against this evidence, Patent Owner directs us to the report in Voswinckel JESC that "there were no significant adverse effects" at the lowest treprostinil concentration but that "mild and transient" "[h]eadache, cough or bronchoconstriction were observed" in some patients at higher doses, and that one patient at Voswinckel JESC's highest treprostinil dose "complained of major headache for 1 hour." Ex. 1007, 7; *see* PO Resp. 37–38. As Patent Owner puts it, "Voswinckel JESC warns in its Conclusion that 'at a concentration of 16 µg/ml, near maximal pulmonary vasodilation is achieved without adverse effects' but '[a]t higher doses, local and systemic side effects may occur.'" PO Resp. 37–38 (quoting Ex. 1007, 7). Because Petitioner's proffered reason to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA requires an increase in treprostinil concentration in order to administer the full dose in three breaths, Patent Owner argues that Voswinckel JESC's warning about side effects at higher doses would have persuaded a person of ordinary skill in the art not to pursue such a course. *Id.*

The preponderance of the evidence supports Petitioner's position. Patent Owner is correct that Voswinckel JESC notes that side effects could occur more frequently at higher doses than at lower doses. Ex. 1007, 7. But there is considerable evidence of record that a person of ordinary skill in the art would not have avoided increasing Voswinckel JESC's dose due to the side effects reported in Voswinckel JESC. First, Dr. Hill testifies that "[p]otential side effects are always weighed against potential clinical benefit, and pulmonary arterial hypertension is a serious, life-threatening disease where physicians and patients are more willing to tolerate side effects . . . to obtain clinical benefit." Ex. 1106 ¶ 74. Second,

Dr. Waxman testifies that "[u]sually the headache goes away" and "there are things that can be done to help ameliorate the cough so in general we are able to get over that issue." Ex. 1108, 101:19–102:10. Together with Voswinckel JESC's description of potential side effects as "mild and transient," this evidence supports a finding that a person of ordinary skill in the art would not have been deterred from pursuing the course that is supported by the evidence to which Petitioner directs us.

With respect to reasonable expectation of success, Petitioner argues that a person of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA because Voswinckel JAHA teaches that "[t]olerability is excellent" for its short-duration, high-concentration treprostinil inhalation therapy. Pet. 33 (citing Ex. 1008, 3). Other than the argument discussed above about side effects reported in Voswinckel JESC, Patent Owner does not raise any timely counter to this argument.[8] PO Resp. 10–40. The record supports Petitioner's argument. Ex. 1008, 3.

---

[8] In the Sur-Reply, Patent Owner raises for the first time three arguments against a reasonable expectation of success. Sur-Reply 21–22 (arguing that a person of ordinary skill in the art would not expect success in delivering Voswinckel JESC's dose over Voswinckel JAHA's three breaths because (1) it would require "increas[ing] the number [of] doses per day," (2) Voswinckel JAHA "lacked any placebo arm," and (3) Voswinckel JESC and Voswinckel JAHA used patients with differing pulmonary vascular resistances). "A sur-reply may only respond to arguments raised in the corresponding reply." 37 C.F.R. § 42.23(b). Petitioner's Reply did not raise any argument regarding a reasonable expectation of success. Reply

Accordingly, Petitioner has shown by a preponderance of the evidence that a person of ordinary skill in the art would have had a reason to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA and that they reasonably would have expected to succeed in doing so.

c. Objective Indicia of Nonobviousness

Patent Owner directs us to evidence of three objective indicia that Patent Owner argues show the nonobviousness of the challenged claims. PO Resp. 55–62. Petitioner argues that the claims would have been obvious despite the evidence to which Patent Owner directs us. Reply 23–27.

(1) Unexpected Results

First, Patent Owner directs us to evidence that allegedly demonstrates that the challenged claims would have been nonobvious because they "unexpectedly achieved a therapeutically effective dose that was well tolerated" despite the fact that such "high doses of treprostinil were known in the art to produce dose-limiting side effects." PO Resp. 55. According to Patent Owner, the challenged claims "produce[d] a new and unexpected result which is different in kind and not merely in degree from the results of the prior art," which is evidence of those claims' nonobviousness. *Id.* at 55–57 (quoting *In re Aller*, 220 F.2d 454, 456 (CCPA 1955)). Specifically, Patent Owner argues that the inhaled treprostinil dose recited in the challenged claims represented an increase of "an order of magnitude" over "the maximal tolerated dose" of "intravenous epoprostenol" or "intravenous

---

1–27. Therefore, we do not consider these newly raised arguments as they exceed the proper scope of the Sur-Reply.

treprostinil." *Id.* at 56. Similarly, Patent Owner argues that the challenged claims cover doses of inhaled treprostinil higher than a dose of inhaled iloprost that many patients were unable to tolerate. *Id.* at 56–57.

"[U]nexpected results must establish . . . a difference between the results obtained and those of the closest prior art." *Bristol-Myers Squibb v. Teva Pharms. USA*, 752 F.3d 967, 977 (Fed. Cir. 2014). Petitioner argues that the prior art over which Patent Owner argues the challenged claims showed unexpected results is not the closest prior art. Reply 24. We agree. As noted above, Patent Owner argues that the challenged claims show unexpected results over inhaled iloprost, intravenous epoprostenol, and intravenous treprostinil. PO Resp. 55–57. But the challenged claims recite inhaled treprostinil, and, as discussed above, inhaled treprostinil is taught by each of the '212 patent, Voswinckel JESC, and Voswinckel JAHA. Ex. 1001, 18:22–44; Ex. 1006, code (57); Ex. 1007, 7; Ex. 1008, 3; Ex. 1035, 582. Patent Owner does not even allege that the results of the challenged claims are unexpected over these references.[9] Accordingly, we find that the evidence of record does not establish that the challenged claims produced a result that was unexpected over the closest prior art.

[9] Patent Owner argues that Voswinckel JESC and Voswinckel JAHA are not prior art to the '793 patent. PO Response 44–55; Sur-Reply 2–11, 25. As discussed above, however, Petitioner has shown by a preponderance of the evidence that these references qualify as prior art.

(2) Copying

Second, Patent Owner directs us to evidence that allegedly demonstrates that the challenged claims would have been nonobvious because Petitioner copied Patent Owner's product, Tyvaso, which is an embodiment of the challenged claims, when Petitioner developed its product, LIQ861. PO Resp. 57–61.

"[F]or objective indicia of nonobviousness to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *Lectrosonics, Inc. v. Zaxcom, Inc.*, IPR2018-01129, Paper 33, 32 (PTAB Jan. 24, 2020) (precedential) (citing *ClassCo, Inc. v. Apple, Inc.*, 838 F.3d 1214, 1220 (Fed. Cir. 2016)). A patentee is entitled to a presumption of nexus "when the patentee shows that the asserted objective evidence is tied to a specific product and that product 'embodies the claimed features, and is coextensive with them.'" *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019) (quoting *Polaris Indus., Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1072 (Fed. Cir. 2018) (quoting *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1130 (Fed. Cir. 2000))).

Here, Patent Owner does not allege, let alone "show[]" as required by *Fox Factory*, that Petitioner's LIQ861 product "is coextensive with" the features claimed in the '793 patent. 944 F.3d at 1373; *see* PO Resp. 57–61; Sur-Reply 26. Patent Owner does allege that the LIQ861 product embodies the challenged claims, PO Resp. 58–61, and we presume for purposes of our analysis that Patent Owner's allegation on this issue is correct. But *Fox Factory* requires both a showing that the product in question embodies the

claims and a showing that the product in question is coextensive with the claims, and Patent Owner satisfies at most one of those two requirements. Accordingly, we find that a presumption of nexus is inappropriate.

"A finding that a presumption of nexus is inappropriate does not end the inquiry into secondary considerations." *Fox Factory*, 944 F.3d at 1373. "To the contrary, the patent owner is still afforded an opportunity to prove nexus by showing that the evidence of secondary considerations is the 'direct result of the unique characteristics of the claimed invention.'" *Id.* at 1373–74 (quoting *In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996)). "Where the offered secondary consideration actually results from something other than what is both claimed and *novel* in the claim, there is no nexus to the merits of the claimed invention," meaning that "there must be a nexus to some aspect of the claim not already in the prior art." *In re Kao*, 639 F.3d 1057, 1068–69 (Fed. Cir. 2011) (emphasis in original).

On the other hand, there is no requirement that "objective evidence must be tied exclusively to claim elements that are not disclosed in a particular prior art reference in order for that evidence to carry substantial weight." *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1331 (Fed. Cir. 2016). A patent owner may show, for example, "that it is the claimed combination as a whole that serves as a nexus for the objective evidence; proof of nexus is not limited to only when objective evidence is tied to the supposedly 'new' feature(s)." *Id.* Ultimately, the fact finder must weigh the secondary considerations evidence presented in the context of whether the claimed invention as a

whole would have been obvious to a skilled artisan. *Id.* at 1331–32.

Here, Patent Owner directs us to several pieces of evidence that it contends show the LIQ861 product has a nexus to the challenged claims. First, as noted above, Patent Owner argues that LIQ861 embodies those claims. PO Resp. 58–61. Second, Patent Owner notes that "[t]he pharmacokinetics and bioavailability of a 79.5 microgram capsule dose [of LIQ861] was directly compared [by Petitioner] with Patent Owner's commercial product," demonstrating that "Petitioner's commercial product had comparable treprostinil bioavailability with Tyvaso® when delivered in a similar dosage range." *Id.* at 57–58 (citing Ex. 2085). Third, Patent Owner directs us to the new drug application Petitioner filed with the FDA, "relying in part on FDA's previous findings of efficacy and safety of Tyvaso® for the treatment of PAH." *Id.* at 58 (citing Ex. 2089, 3).

Taking these pieces of evidence in reverse order, we note first that the new drug application for LIQ861 was filed "under the 505(b)(2) regulatory pathway." *Id.*; *see also* Reply 25; Ex. 2089, 3. As Petitioner notes, Reply 25, and as Patent Owner does not dispute, Sur-Reply 26, applications for drugs under this pathway do not necessarily copy all aspects of the original drug, but they may rely on the investigations that showed the safety and efficacy of the original drug that uses the same active ingredient. 21 U.S.C. § 355(b)(2). In this respect, they differ from applications under the § 505(j) regulatory pathway, under which the new drug must generally have the same "active ingredient," "route of administration," "dosage form," "strength," and "labeling" as the original drug. 21 U.S.C. § 355(j)(2). Because

the challenged claims here recite limitations requiring administration by inhalation of a particular amount of treprostinil in a particular number of breaths (and in some cases using a particular type of device and with the drug in a particular form), evidence that Petitioner merely relied on previous studies of the safety and efficacy of the recited active ingredient is not particularly strong evidence of copying.

Next, we consider the evidence that Petitioner compared the pharmacokinetics and bioavailability of its LIQ861 product with those of Patent Owner's Tyvaso product. Ex. 2085. Patent Owner argues that this evidence shows that "Petitioner's commercial product had comparable treprostinil bioavailability with Tyvaso® when delivered in a similar dosage range." PO Resp. 57–58. Regardless of whether an objective indicium of nonobviousness has its nexus to a single "aspect of the claim not already in the prior art," *Kao*, 639 F.3d at 1068–69, or to "the claimed combination as a whole," *WBIP*, 829 F.3d at 1331, it still must have some nexus to the claim in question. The challenged claims, however, do not recite any limitations for treprostinil bioavailability or pharmacokinetics. Ex. 1001, 18:22–44. Accordingly, evidence that Petitioner formulated its product to have similar bioavailability and pharmacokinetics to Patent Owner's product is, at most, very weak evidence of copying as to the claims at issue here.

Finally, we consider the evidence that LIQ861 embodies the challenged claims. PO Resp. 58–61. "Not every competing product that arguably falls within the scope of a patent is evidence of copying; otherwise, 'every infringement suit would automatically confirm the nonobviousness of the patent.'"

Wyers v. Master Lock Co., 616 F.3d 1231, 1246 (quoting *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1325 (Fed. Cir. 2004)). Proof of copying requires "actual evidence of copying efforts as opposed to mere allegations regarding similarities between the accused product and a patent." *Liqwd, Inc. v. L'Oreal USA, Inc.*, 941 F.3d 1133, 1137–38 (Fed. Cir. 2019). Thus, evidence that LIQ861 embodies the challenged claims is not evidence that could, without more, support a finding that Petitioner copied Patent Owner's patented method. As discussed above, to the extent there is any evidence of what *Liqwd* refers to as "copying efforts" beyond mere similarity between LIQ861 and the challenged claims, that evidence shows that Petitioner copied only features that appear in the prior art, are not recited in the challenged claims, or both. Accordingly, we do not find that Patent Owner has shown that Petitioner copied the method of the challenged claims.

(3) Long-Felt and Unmet Need

Patent Owner directs us to evidence that allegedly demonstrates that the challenged claims would have been nonobvious because "[t]he claimed invention of the '793 patent satisfies a long-felt unmet need in the treatment of pulmonary hypertension." PO Resp. 61–62; *see* Sur-Reply 26. Patent Owner relies on three separate theories to demonstrate this long-felt need. First, in the Response, Patent Owner argues that the approval of inhaled treprostinil as the first treatment for "pulmonary hypertension associated with interstitial lung disease" satisfied "a completely unmet medical need." PO Resp. 61–62 (quoting Ex. 2056, 105:6–8). Second, also in the Response, Patent Owner argues that Petitioner admitted that its LIQ861

product "fulfill[ed] a significant unmet need for PAH patients by maximizing the therapeutic benefits of treprostinil by safely delivering doses to the lungs in 1 to 2 breaths using a discreet, convenient, easy-to-use inhaler." *Id.* at 62 (quoting Ex. 2085). Third, in the Sur-Reply, Patent Owner argues that its Tyvaso product satisfied a need for an "inhaled treatment for pulmonary hypertension" that avoided the "inconvenient dosing and side effects of Ventavis," the only previously approved treatment. Sur-Reply 26 (citing Ex. 1002 ¶ 42; Ex. 1108, 44:19–21, 49:17–50:10; Ex. 2055, 28:22–29:20). Each of these arguments fails for a different reason.

We begin with Patent Owner's third argument, that Tyvaso satisfied a need for an inhaled treatment that avoided the dosing problems and side effects of Ventavis. Patent Owner offers this argument for the first time in the Sur-Reply. *Id.* "A sur-reply may only respond to arguments raised in the corresponding reply." 37 C.F.R. § 42.23(b). "'Respond,' in the context of 37 C.F.R. § 42.23(b), does not mean proceed in a new direction with a new approach as compared to the positions taken in a prior filing." Patent Trial and Appeal Board Consolidated Trial Practice Guide 74 (Nov. 2019), available at https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf. As discussed in more detail below, in its prior filings, Patent Owner's only positions with respect to long-felt need were (1) that the patented method satisfied a need for a treatment for pulmonary hypertension associated with interstitial lung disease and (2) that Petitioner admitted that its product satisfied a need. PO Resp. 61–62. Neither of those positions related to a need for a treatment that avoided the problems associated with Ventavis. *Id.* Accordingly, Patent Owner's argu-

ment in the Sur-Reply is a new argument that we do not consider further.

Next, we consider Patent Owner's argument that the method of the '793 patent provided the first treatment for pulmonary hypertension associated with interstitial lung disease. *Id.* Even if this is true, it is extremely weak evidence of the nonobviousness of the claims at issue because those claims do not cover treatment of pulmonary hypertension associated with interstitial lung disease. There are multiple groups of pulmonary hypertension conditions. Ex. 1088, 1. In addition to other groups not relevant here, these groups include "WHO Group 1," or "[p]ulmonary arterial hypertension," and "WHO Group 3," or "[p]ulmonary hypertension associated with interstitial lung disease." *Id.* Patent Owner's declarant, Dr. Waxman, testifies that all pulmonary hypertension groups other than Group 1 fall outside the scope of the claims of the '793 patent. Ex. 1132, 116:9–119:12. Dr. Hill agrees. Ex. 1106 ¶ 100. Thus, to the extent the challenged claims satisfied a long-felt and unmet need for a treatment for pulmonary hypertension associated with interstitial lung disease, Patent Owner has not shown that that need is tied to any limitation of the challenged claims or to any challenged claim as a whole.

Finally, we consider Patent Owner's argument that Petitioner admitted that its LIQ861 product "fulfill[ed] a significant unmet need for PAH patients by maximizing the therapeutic benefits of treprostinil by safely delivering doses to the lungs in 1 to 2 breaths using a discreet, convenient, easy-to-use inhaler." PO Resp. 62 (quoting Ex. 2085). "Evidence of a long- felt but unresolved need can weigh in favor of the non-obviousness of an invention because it is

reasonable to infer that the need would not have persisted had the solution been obvious." *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1056 (Fed. Cir. 2016). Patent Owner directs us to two pieces of evidence. First, Patent Owner directs us to Exhibit 2085, which states that LIQ861 "fulfill[ed] a significant unmet need for PAH patients by maximizing the therapeutic benefits of treprostinil by safely delivering doses to the lungs in 1 to 2 breaths using a discreet, convenient, easy-to-use inhaler." Ex. 2085, 1. This demonstrates that Petitioner believed its product satisfied a particular "significant unmet need," but it does not demonstrate how long that need persisted. *Id.* Second, Patent Owner directs us to page F-7 of Exhibit 2089, but this page does not address the filling of any need by LIQ861. Ex. 2089, F-7. Thus, Patent Owner does not show that any previously unmet need satisfied by LIQ861 was a need that had persisted, as required by *Apple v. Samsung*. Accordingly, we do not find that Patent Owner has shown that the patented method satisfied any previously unmet and long-felt need.

d. Dependent Claims

Claims 2–8 of the '793 patent depend directly or indirectly from claim 1. Ex. 1001, 18:32–45. Petitioner argues that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests the additional limitations of these claims. Pet. 41–46. Patent Owner does not dispute these arguments, except with respect to claims 4, 6, and 7. PO Resp. 38–40.

We have reviewed the evidence cited by Petitioner with respect to dependent claims 2, 3, 5, and 8, and we are persuaded that Petitioner has shown by a preponderance of the evidence that the combination

of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests the subject matter of these claims. For example, claim 2 depends from claim 1 and recites a further limitation that requires that "the inhalation device [be] a soft mist inhaler," and Petitioner directs us to evidence that soft mist inhalers were known in the prior art, as well as evidence that soft mist inhalers were known to be suitable for inhaled delivery of drugs in a small number of breaths. Ex. 1001, 7:33–39, 18:32–33; Ex. 1002 ¶¶ 106–110; Ex. 1004 ¶¶ 66–71; Ex. 1006, 5:30–32; Ex. 1034, 175.

The parties dispute the obviousness of claims 4, 6, and 7. Claim 4 depends from claim 1 and recites a limitation requiring that "the inhalation device [be] a dry powder inhaler." Ex. 1001, 18:36–37. Claim 6 depends from claim 4 and adds a limitation requiring that "the formulation [be] a powder." *Id.* at 18:40–41. Claim 7 depends from claim 6 and adds a limitation requiring that "the powder comprise[] particles less than 5 micrometers in diameter." *Id.* at 18:42–43. Petitioner argues that each of these limitations is taught or suggested by the '212 patent. Pet. 43–45 (citing Ex. 1006, 5:30–32, 5:37–41, 14:19–21; Ex. 1002 ¶¶ 116–117; Ex. 1004 ¶¶ 77–80; Ex. 1038, 311). Patent Owner argues that Petitioner's obviousness argument with respect to these claims is inconsistent with Petitioner's argument in the parallel District Court proceeding that these claims are not enabled. PO Resp. 38–40. Specifically, Patent Owner argues that Dr. Gonda's testimony here that a person of ordinary skill in the art "would have had a reasonable expectation of success that the 'powder' disclosed and claimed in the '212 Patent could be 'inhaled' by a patient using a dry powder inhaler" contradicts Dr. Gonda's testimony in District Court that a person of

ordinary skill in the art "would be unable to formulate a treprostinil powder suitable for administration via a dry powder inhaler for [pulmonary hypertension] patients without excessive experimentation." PO Resp. 38–39 (quoting Ex. 1004 ¶ 80; Ex. 2091, 40–61). Because Dr. Gonda's District Court testimony is more "lengthy" than his testimony here, Patent Owner argues that the District Court testimony is more reliable and that, accordingly, we should not rely on Dr. Gonda's testimony here. *Id.* at 40.

Dr. Gonda's testimony here provides support for Petitioner's argument that a person of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA in order to arrive at the invention of claims 4, 6, and 7. Ex. 1004 ¶ 80. Reasonable expectation of success is a separate inquiry from enablement. *UCB, Inc. v. Accord Healthcare, Inc.*, 890 F.3d 1313, 1327 (Fed. Cir. 2018) (finding no "authority for the proposition that the presumption of" enablement of prior art "precludes . . . finding that there was no reasonable expectation of success"). Accordingly, the mere fact that Dr. Gonda testifies to a lack of enablement in one forum and to the presence of a reasonable expectation of success in a second forum does not render unreliable the testimony in either forum. Therefore, we credit the unrebutted testimony of Dr. Gonda that a person of ordinary skill in the art "would have had a reasonable expectation of success that the 'powder' disclosed and claimed in the '212 Patent could be 'inhaled' by a patient using a dry powder inhaler." Ex. 1004 ¶ 80. In addition, Dr. Gonda's testimony in this proceeding is supported by a citation to Ex. 1038, an October 2005 article that states that dry powder inhalers "are a widely accepted inhaled delivery

dosage form," as well as to Ex. 1019, an article stating that 14 separate dry powder inhalers were approved in the United States by 2006. Ex. 1019, 33; Ex. 1038, 1311. This evidence provides us with an additional reason to credit Dr. Gonda's testimony as to reasonable expectation of success.

Moreover, even if there were some connection between enablement and reasonable expectation of success, Patent Owner concedes that the '212 patent enables its own claims. Tr. 43:6–50:9. In other words, the '212 patent provides enough information for a person of ordinary skill in the art to have made and used the invention defined by the claims of the '212 patent. *See* 35 U.S.C. § 112. That invention includes "[a] method for treating pulmonary hypertension in a mammal comprising delivering to said mammal an effective amount of [treprostinil] or its pharmaceutically acceptable salt or ester by inhalation," wherein the treprostinil "is inhaled in powder form comprising particles less than 10 micrometers in diameter." Ex. 1006, 14:9–12, 14:19–21. To the extent that, despite *UCB*, 890 F.3d at 1327, there remains any connection at all between a reasonable expectation of success and enablement, the fact that a person of ordinary skill in the art was enabled to make and use this invention presumably would have rendered that person more likely to expect success in achieving the similar invention of claims 4, 6, and 7 of the '793 patent.

Further, as discussed above with respect to the reason to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA, Petitioner directs us to other evidence that a person of ordinary skill in the art would have had a reasonable expectation of success.

For all these reasons, we determine that Petitioner has shown by a preponderance of the evidence that a person of ordinary skill in the art would have had a reason to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA and would have had a reasonable expectation of success in doing so in order to arrive at the invention of the challenged claims, including claims 4, 6, and 7.

Thus, we move on to whether the prior art teaches or suggests the additional limitations of claims 4, 6, and 7. Petitioner argues that the '212 patent teaches or suggests each of these limitations, and Patent Owner does not dispute that argument. Pet. 43–45; PO Resp. 38–40. Claim 4 recites a limitation requiring that "the inhalation device [be] a dry powder inhaler." Ex. 1001, 18:36–37. The '212 patent teaches using an "inhaler" to deliver treprostinil, that "solid formulations, usually in the form of a powder, may be inhaled in accordance with the present invention," and that treprostinil "is inhaled in powder form." Ex. 1006, 5:30–32, 5:37–39, 14:19–21. Dr. Hill testifies that a person of ordinary skill in the art would have known that the "inhaler" used to deliver the "powder" of the '212 patent was a dry powder inhaler. Ex. 1002 ¶ 116. Claim 6 depends from claim 4 and adds a limitation requiring that "the formulation [be] a powder." Ex. 1001, 18:40–41. The '212 patent teaches that "solid formulations, usually in the form of a powder, may be inhaled in accordance with the present invention," as well as that treprostinil "is inhaled in powder form." Ex. 1006, 5:37–39, 14:19–21. Claim 7 depends from claim 6 and adds a limitation requiring that "the powder comprise[] particles less than 5 micrometers in diameter." Ex. 1001, 18:42–43. The '212 patent teaches that "the particles are preferably less than 10

micrometers in diameter, and more preferably, less than 5 micrometers in diameter." Ex. 1006, 5:39–41. Accordingly, Petitioner has shown by a preponderance of the evidence that the '212 patent teaches or suggests the additional limitations of claims 4, 6, and 7 of the '793 patent.

e. Conclusion

As discussed above, Petitioner has shown by a preponderance of the evidence that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests the subject matter of claims 1–8. Petitioner also has shown by a preponderance of the evidence that a person of ordinary skill in the art would have had a reason to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA and would have had a reasonable expectation of success in doing so to arrive at the invention of the challenged claims. In addition, the preponderance of the evidence shows that there is at most very weak evidence of objective indicia of nonobviousness, including unexpected results, copying, and long-felt but unmet need. Weighing together the evidence of the prior art teaching or suggesting the subject matter of the claims, of a reason to combine the teachings of the prior art with a reasonable expectation of success, and of objective indicia of nonobviousness, we conclude that Petitioner has demonstrated that claims 1–8 of the '793 patent would have been obvious over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA and, accordingly, that those claims are unpatentable.

C. Asserted Obviousness over '212 Patent and Voswinckel JESC

Petitioner argues that claims 1–8 would have been obvious over the combination of the '212 patent and Voswinckel JESC. Pet. 46–50. Because Petitioner has shown by a preponderance of the evidence that all of the challenged claims would have been obvious over the similar combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA, we need not reach this asserted ground.

D. Grounds Relying on Ghofrani or Voswinckel 2006

Petitioner argues that claim 1 was anticipated by Ghofrani; that claims 1, 3, and 8 would have been obvious over the combination of Voswinckel JAHA and Ghofrani; that claims 1 and 3 were anticipated by Voswinckel 2006; and that claims 2 and 4–8 would have been obvious over the combination of Voswinckel 2006 and the '212 patent. Pet. 50–64. Patent Owner argues that each of these grounds fails because Petitioner fails to show sufficiently that Ghofrani and Voswinckel 2006 qualify as prior art. PO Resp. 44–54. Petitioner disagrees, arguing that these references qualify as prior art under 35 U.S.C. § 102(a). Pet. 25–30.

In the institution decision, we determined that, on the preliminary record available at the time, Petitioner had not shown that either Ghofrani or Voswinckel 2006 qualified as prior art. Inst. Dec. 37–43. Since that decision, Petitioner has neither supplemented the record nor made any additional arguments on this issue. Reply 1–27. During the hearing, Petitioner did not agree that it had abandoned its argument on the grounds asserting

Ghofrani or Voswinckel 2006. Tr. 35:13–36:10. Nevertheless, in the absence of any new evidence or argument, we have been directed to nothing that persuades us to reach any decision other than we reached initially. Accordingly, our analysis below mirrors the analysis we conducted in the institution decision.

1. Prior-Art Status of Ghofrani

Ghofrani is an article published in the German journal Herz in June 2005, less than one year before the priority date of the '793 patent. Pet. 25; Ex. 1010, 9; Ex. 1036 ¶¶ 47–55. Petitioner argues that Ghofrani is prior art to the '793 patent under 35 U.S.C. § 102(a). Pet. 25–27. Patent Owner disagrees, arguing that Petitioner has not shown sufficiently that Ghofrani is "by others" under § 102(a). PO Resp. 44–51.

As both parties acknowledge, establishing prior-art status under § 102(a) requires showing that the reference is "by others," meaning that it was authored by an entity different from the entity that invented the challenged patent. Pet. 26–27; PO Resp. 44–46; *see Lacks Industries, Inc. v. McKechnie Vehicle Components USA, Inc.*, 322 F.3d 1335, 1346 (Fed. Cir. 2003) ("it is well-settled law that an inventor's own disclosure will not anticipate his later invention" unless published more than one year prior to the priority date (internal quotation marks omitted)).

The authors of Ghofrani are "Hossein Ardeschir Ghofrani, Robert Voswinckel, Frank Reichenberger, Friedrich Grimminger, [and] Werner Seeger." Ex. 1010, 9. The inventors of the '793 patent are Horst Olschewski, Robert Roscigno, Lewis J. Rubin, Thomas Schmehl, Werner Seeger, Carl Sterritt, and

Robert Voswinckel. Ex. 1001, code (72). Thus, there are, as Petitioner argues, "inventors listed on the '793 Patent that are not listed as authors on Ghofrani, and vice versa." Pet. 26. Specifically, Ghofrani, Reichenberger, and Grimminger authored the Ghofrani reference but were not inventors of the '793 patent; and Olschewski, Roscigno, Rubin, Schmehl, and Sterritt were inventors of the '793 patent but not authors of the Ghofrani reference.

Petitioner argues that these differences alone are sufficient to show that Ghofrani is "by others." *Id.* at 26–27. We agree that it is possible, depending on the state of the rest of the evidence of record, for any difference between the authors of an alleged prior-art reference and the inventors of a challenged patent to render the reference "by others" for purposes of § 102(a). *See, e.g.*, *In re Katz*, 687 F.2d 450, 455 (CCPA 1982) ("ambiguity [was] created by the printed publication" where authors included people not named as inventors); *cf. In re Land*, 368 F.2d 866, 877 (CCPA 1966) (for purposes of § 102(e), reference authored by one co-inventor was "by another").

That said, it is not always sufficient for Petitioner merely to show a difference between a list of authors and a list of inventors. Where the record contains evidence that the reference was derived entirely from the work of the inventors or at least one joint inventor, this evidence may be sufficient to show that the reference is not "by others" for purposes of § 102(a). *Katz*, 687 F.2d at 455–56 (finding inventor's declaration of sole inventorship sufficient to render reference authored by inventor and others not "by others"). Although the testimony of an inventor that the reference in question was derived from the inventors' work may be sufficient on its own, at least

where it is not "a mere pro forma restatement of the oath in [the inventor's] application," affidavits from the other authors disclaiming the invention are particularly strong evidence that the reference is not "by others." *Id.* ("Submission of such affidavits or declarations would have ended the inquiry"). Here, for the reasons discussed below, the preponderance of the evidence persuades us that, despite the differences between its list of authors and the list of the inventors of the '793 patent, Ghofrani is not "by others" for purposes of § 102(a).

Petitioner's first argument that Ghofrani is "by others" is that there are people who are authors of Ghofrani who are not inventors of the '793 patent. Pet. 26. But Dr. Seeger, one of the inventors of the '793 patent, as well as an author of Ghofrani, describes the roles of the other authors of Ghofrani, explaining that Dr. Ghofrani drafted the portion of the article "relating to phosphodiesterase inhibitors," that Drs. Reichenberger and Grimminger drafted the portion of the article relating to "the use of selective endothelin A receptor agonists for treating pulmonary hypertension," and that he and Dr. Voswinckel—another co-inventor—drafted the portion of the article relating to "the use of inhaled iloprost and inhaled treprostinil for treatment of pulmonary hypertension," the only portion on which Petitioner's unpatentability case rests. Ex. 2003 ¶¶ 4–8. Dr. Seeger's testimony is corroborated by the testimony of Drs. Ghofrani, Reichenberger, and Grimminger, each of whom testifies that they "did not make material contributions to" the portion of the Ghofrani reference relating to inhaled treprostinil. Ex. 2004 ¶¶ 4–5; Ex. 2005 ¶¶ 4–5; Ex. 2006 ¶¶ 4–5. This is precisely the type of testimony that the *Katz* court held should "end[] the inquiry" into whether Ghofrani

was "by others." 687 F.2d at 455–56. Accordingly, this evidence overcomes Petitioner's argument that the difference between the Ghofrani authors and the inventors of the '793 patent is sufficient to show that Ghofrani is "by others."

Petitioner also argues that the failure to include some of the inventors of the '793 patent—Olschewski, Roscigno, Rubin, Schmehl, and Sterritt—as authors of Ghofrani renders Ghofrani "by others." Pet. 26–27. But "the fact that a reference does not list any co-inventors as authors . . . is certainly not dispositive in itself." *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 969 (Fed. Cir. 2014); *see* MPEP § 2132.01(I) ("An inventor's or at least one joint inventor's disclosure of his or her own work within the year before the application filing date cannot be used against the application as prior art under pre-AIA 35 U.S.C. 102(a)."). Moreover, Dr. Seeger explains the roles of the other named inventors in designing trials and clinical studies leading to the patent application. Ex. 2003 ¶¶ 22–27. In particular, Dr. Seeger testifies that the Ghofrani reference did not report on the details of the studies and trials that were in part designed by these other authors, explaining why they did not contribute to writing Ghofrani, even though they were involved in the related work that gave rise to the '793 patent. *Id.* ¶¶ 11–12. Dr. Seegar further explains that, "any study that formed the basis of our discussion of inhaled trepostinil in [Ghofrani and two other references] was performed by me in conjunction with my ongoing collaboration with Drs. Voswinckel, Olschewski, Rubin, Schmehl, Sterrit, and Roscigno." *Id.* ¶ 12. Again, then, the preponderance of the evidence supports a determination that Ghofrani is not "by others" for purposes of § 102(a).

2. Prior-Art Status of Voswinckel 2006

The issues and arguments regarding Voswinckel 2006 are quite similar to those discussed above regarding Ghofrani. Petitioner argues that Voswinckel 2006 qualifies as prior art under § 102(a) and that it is "by others" both because some of its authors—specifically, Ghofrani and Grimminger—are not inventors of the '793 patent and because some inventors of the '793 patent—specifically, Olschewski, Roscigno, Rubin, Schmehl, and Sterritt—are not authors of Voswinckel 2006. Pet. 27–30. Patent Owner disagrees, pointing to the testimony of Drs. Seeger, Ghofrani, and Grimminger explaining the role that the other inventors of the '793 patent played, as well as making clear that neither Ghofrani nor Grimminger authored the portion of Voswinckel 2006 that is relevant as prior art. PO Resp. 44–46, 51–54; Ex. 2003 ¶¶ 20–21 (describing the roles of Drs. Ghofrani and Grimminger, explaining that they "did not participate in the design of any of the studies, did not select the dosing regimen, and did not conduct analysis of patient results discussed in . . . Voswinckel 2006"); 19 ("any study that formed the basis of our discussion of inhaled treprostinil in this reference was performed by me in connection with my ongoing collaboration with [the other inventors]").

For the same reasons discussed above with respect to Ghofrani, we determine that the preponderance of the evidence shows that Petitioner has not shown sufficiently that Voswinckel 2006 is "by others."

3. Conclusion

For the reasons discussed above, Petitioner has not shown that either Ghofrani or Voswinckel 2006 qualifies as prior art. Accordingly, Petitioner has not

shown the unpatentability of any challenged claim on any ground that relies on either Ghofrani or Voswinckel 2006.

E. Motions to Exclude Evidence

Each party filed a motion to exclude evidence. Paper 65; Paper 66. We consider each motion separately below.

1. Petitioner's Motion to Exclude

Petitioner moves to exclude Exhibits 2092, 2100, 2101, 2102, and 2103 as not authenticated and, for Ex. 2092, as incomplete. Paper 65, 1. Petitioner also moves to exclude the portions of Patent Owner's Sur-Reply that rely on these exhibits. *Id.*

We do not rely on any of the exhibits Petitioner challenges in reaching our decision in this case. Accordingly, we dismiss Petitioner's motion to exclude as moot.

2. Patent Owner's Motion to Exclude

Patent Owner moves to exclude Exhibits 1037, 1114, 1117, and 1120 as hearsay and, for Ex. 1037, as not authenticated, irrelevant, and lacking the original writing. Paper 66, 2. Patent Owner also moves to exclude Exhibits 1029, 1050, 1066, 1074, and 1078 as not authenticated. *Id.* Patent Owner moves to exclude Exhibit 1087 as lacking personal knowledge and as irrelevant. *Id.* Patent Owner also moves to exclude portions of Exhibit 1112 as not based on sufficient facts and analysis. *Id.* Further, Patent Owner moves to exclude the portions of Petitioner's Petition and Reply, as well as the portions of Exhibits 1002 and 1004, that cite these exhibits. *Id.* at 2–3.

We do not rely on any of the exhibits or portions of exhibits Patent Owner moves to exclude in reaching our decision in this case, with two exceptions: paragraphs 36 and 42 of Ex. 1002, which cite Ex. 1029, and paragraph 56 of Ex. 1004, which Patent Owner argues cites Ex. 1029, Ex. 1050, and Ex. 1066. We dismiss as moot Patent Owner's motion to exclude, except as to these paragraphs of Exhibits 1002 and 1004. We discuss the remaining portions of Patent Owner's motion to exclude below.

a. Paragraphs 36 and 42 of Exhibit 1002

Patent Owner moves to exclude paragraphs 36 and 42 of Exhibit 1002 because they rely on Exhibit 1029, which Patent Owner argues lacks authentication. Paper 66, 2–3.

Certain items are self-authenticating under Federal Rule of Evidence ("FRE") 902, and, for items that are not self-authenticating, FRE 901 provides that "the proponent [of the evidence in question] must produce evidence sufficient to support a finding that the item is what the proponent claims it is." Fed. R. Evid. 901(a). The evidence showing "that the items is what the proponent claims it is" may include "[t]estimony that an item is what it is claimed to be," or "[t]he appearance, contents, substance, internal patterns, or other distinctive characteristics of the item, taken together with all the circumstances," among other things. Fed. R. Evid. 901(b).

Here, Dr. Hill, Petitioner's declarant, testifies three times that Exhibit 1029 is the "Ventavis Label 2004." Ex. 1002 ¶¶ 36, 41, 42. Dr. Gonda, another declarant for Petitioner, testifies that Exhibit 1029 is the "Ventavis (iloprost) Label." Ex. 1004 ¶ 56 n.4. Dr. Waxman, Patent Owner's declarant, cites to Exhibit

1029 twice as support for the approved dose for, and side effects experienced by, patients taking Ventavis. Ex. 2052 ¶ 100. The "appearance, contents, substance, internal patterns, [and] other distinctive characteristics," Fed. R. Evid. 901(b), of Ex. 1029 confirm the testimony of Drs. Hill, Gonda, and Waxman. The document contains sections titled "description," "clinical pharmacology," "indications and usage," "contraindications," "warnings," "precautions," "adverse reactions," "overdosage," "dosage and administration," "how supplied," "storage," and "patient information," with each section providing information related to "Ventavis." Ex. 1029, 1–17. This information is consistent with a drug label for Ventavis, which is what Dr. Hill and Dr. Gonda testify, what Dr. Waxman assumes, and what Petitioner argues, Ex. 1029 is. Accordingly, we find that Petitioner has "produce[d] evidence sufficient to support a finding that [Ex. 1029] is what [Petitioner] claims it is." Fed. R. Evid. 901(a). Because Ex. 1029 does not lack authentication, we deny Patent Owner's motion to exclude paragraphs 36 and 42 of Ex. 1002, which cite to Ex. 1029.

b. Paragraph 56 of Exhibit 1004

Patent Owner moves to exclude paragraph 56 of Exhibit 1004 because it relies on Exhibits 1029, 1050, and 1066, all of which Patent Owner argues lack authentication. Paper 66, 2–3. We discuss Exhibit 1029 above, finding that it is sufficiently authenticated. The situation with respect to Exhibits 1050 and 1066 is similar. Dr. Gonda testifies that Ex. 1050 is the "Pulmozyme® Label" and that Ex. 1066 is the "AccuNeb® Label." Ex. 1004 ¶ 56 n.4. Moreover, Dr. Gonda's testimony about what Exhibits 1050 and 1066 are is confirmed by the contents of those

exhibits. Exhibit 1050 contains sections titled "description," "clinical pharmacology," "indications and usage," "contraindications," "warnings," "precautions," "adverse reactions," "overdosage," "dosage and administration," and "how supplied," with each section providing information related to "Pulmozyme." Ex. 1050, 1–2. Exhibit 1066 contains sections titled "description," "clinical pharmacology," "indications and usage," "contraindications," "warnings," "precautions," "adverse reactions," "overdosage," "dosage and administration," "how supplied," "storage," and "patient's instructions for use," with each section providing information related to "AccuNeb." Ex. 1066, 1–2. This information is consistent with drug labels for Pulmozyme and AccuNeb, which is what Dr. Gonda testifies, and what Petitioner argues, Exhibits 1050 and 1066 are. Accordingly, we find that Petitioner has "produce[d] evidence sufficient to support a finding that [Ex. 1050 and Ex. 1066 are] what [Petitioner] claims [they are]." Fed. R. Evid. 901(a). Because Exhibits 1050 and 1066 do not lack authentication, we deny Patent Owner's motion to exclude paragraph 56 of Ex. 1004, which cites to those exhibits.

CONCLUSION[10]

For the reasons discussed above, Petitioner has shown by a preponderance of the evidence that claims 1–8 of the '793 patent are unpatentable.

Claims	35 U.S.C §	Reference(s)/ Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1–8	103(a)	'212 patent, Voswinckel JESC, Voswinckel JAHA	1–8	
1–8	103(a)	'212 patent, Voswinckel JESC[11]		
1	102(a)	Ghofrani		1
1, 3, 8	103(a)	Voswinckel JAHA, Ghofrani		1, 3, 8

[10] 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).

[11] This Final Written Decision does not reach these grounds because Petitioner has proven all challenged claims are unpatentable based on obviousness over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA.

1, 3	102(a)	Voswinckel 2006		1, 3
2, 4–8	103(a)	Voswinckel 2006, '212 patent		2, 4–8
Overall Outcome			1–8	

ORDER

It is hereby

ORDERED that, based on the preponderance of the evidence, claims 1–8 of the '793 patent have been shown to be unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude is dismissed as moot;

FURTHER ORDERED that Patent Owner's Motion to Exclude is denied as to paragraphs 36 and 42 of Exhibit 1002 and as to paragraph 56 of Exhibit 1004;

FURTHER ORDERED that Patent Owner's Motion to Exclude is dismissed as moot in all other respects; and

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

For PETITIONER:

Ivor R. Elrifi
Erik B. Milch
Deepa Kannappan
Sanya Sukduang
Lauren Krickl
Douglas Cheek
Jonathan Davies
COOLEY LLP

ielrifi@cooley.com
emilch@cooley.com
dkannappan@cooley.com
ssukduang@cooley.com
lkrickl@cooley.com
dcheek@cooley.com
jdavies@cooley.com

For PATENT OWNER:

Stephen B. Maebius
George Quillin
Jason N. Mock
Michael Houston
FOLEY & LARDNER LLP
smaebius@foley.com
gquillin@foley.com
jmock@foley.com
mhouston@foley.com

Shaun R. Snader
UNITED THERAPEUTICS CORP.
ssnader@unither.com

Douglas Carsten
April E. Weisbruch
Judy Mohr, Ph.D.
Jiaxiao Zhang
Mandy Kim
Arthur Dykhuis
Amy Mahan
MCDERMOTT WILL & EMERY LLP
dcarsten@mwe.com
aweisbruch@mwe.com
jmohr@mwe.com
jazhang@mwe.com
mhkim@mwe.com
adykhuis@mwe.com
amahan@mwe.com

APPENDIX F

Entered: February 2, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LIQUIDIA TECHNOLOGIES, INC.,

Petitioner,

v.

UNITED THERAPEUTICS CORPORATION,

Patent Owner.

IPR2021-00406
Patent 10,716,793 B2

Before ERICA A. FRANKLIN, CHRISTOPHER M. KAISER, and DAVID COTTA, *Administrative Patent Judges.*

KAISER, Administrative Patent *Judge.*

DECISION

Denying Patent Owner's Request on Rehearing of Final Written Decision

37 C.F.R. § 42.71(d)

INTRODUCTION

Liquidia Technologies, Inc. ("Petitioner") filed a Petition (Paper 2, "Pet.") requesting an *inter partes* review of claims 1–8 of U.S. Patent No. 10,716,793 B2 (Ex. 1001, "the '793 patent"). United Therapeutics Corporation ("Patent Owner") filed a Preliminary Response. Paper 13 ("Prelim. Resp.").

On August 11, 2021, we instituted *inter partes* review of claims 1–8 of the '793 patent on all grounds set forth in the Petition. Paper 18 ("Inst. Dec."). After institution of trial, Patent Owner filed a Response (Paper 29, "PO Resp."), Petitioner filed a Reply (Paper 44), and Patent Owner filed a Sur-Reply (Paper 55). In addition, both parties filed Motions to Exclude Evidence (Papers 65 and 66), Oppositions to their respective opponents' Motions to Exclude (Papers 68 and 69), and Replies in support of their own Motions to Exclude (Papers 71 and 72). At the request of both parties, we held an oral hearing, the transcript of which was entered into the record. Paper 77 ("Tr.").

On July 19, 2022, we issued a Final Written Decision determining that Petitioner had proven by a preponderance of evidence that all the challenged claims were unpatentable. Paper 78 ("Final Dec."). On August 18, 2022, Patent Owner requested rehearing and filed a request that rehearing be conducted by the Precedential Opinion Panel. Paper 79 ("Req. Reh'g"); Paper 80. The request for rehearing by the Precedential Opinion Panel was denied, returning jurisdiction to us to consider the rehearing request itself. Paper 81.

For the reasons discussed below, we deny Patent Owner's Request for Rehearing. Where the present

decision differs from the Final Written Decision, the present decision controls. Otherwise, the Final Written Decision remains in force.

ANALYSIS

A. The Final Written Decision

Petitioner asserted the unpatentability of the challenged claims on six separate grounds. Final Dec. 3–4. Four of those grounds relied on references referred to as Voswinckel 2006 and Ghofrani, both of which we determined did not qualify as prior art. *Id.* at 3–4, 36–41. The remaining two grounds both relied on a reference referred to as Voswinckel JESC, and one of the grounds also relied on a reference referred to as Voswinckel JAHA. *Id.* at 3.

Patent Owner argued during the trial that Petitioner had not proven that either Voswinckel JESC or Voswinckel JAHA had been made publicly accessible early enough to qualify as prior art in the way that Petitioner argued they did. PO Resp. 11–18; Sur-Reply 2–11. Petitioner countered these arguments with several arguments for the public accessibility of Voswinckel JESC and Voswinckel JAHA. Reply 2–9. In particular, Petitioner argued that each of these references was cited in a publicly available journal article that could have served as a research aid to help a person of ordinary skill in the art locate the references. *Id.* at 3–4 (arguing that Voswinckel JESC was cited in Ghofrani), 7–8 (arguing that Voswinckel JAHA was cited in Sulica).

In the Final Written Decision, we were persuaded by Petitioner's argument regarding these research aids. Final Dec. 10–12. Based in part on our determination that these research aids established the public accessibility of Voswinckel JESC and Voswinckel JAHA,

we determined that Petitioner had proven by a preponderance of the evidence that each of the challenged claims would have been obvious over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA. *Id.* at 12–35.

B. The Rehearing Request

Patent Owner seeks rehearing of our Final Written Decision on the ground that we overlooked Patent Owner's argument that the Ghofrani and Sulica research aids had been "published *after* the critical §102(b) date of May 15, 2005." Req. Reh'g 1 (emphasis in original). Patent Owner notes that this argument appeared in the Sur-Reply. *Id.* at 5 (citing Sur-Reply 9). According to Patent Owner, had we not overlooked this argument, we would have determined that Petitioner had not shown that Voswinckel JESC and Voswinckel JAHA were publicly accessible in the way necessary to treat them as prior art to the '793 patent. *Id.* at 5–14.

When it requested rehearing, Patent Owner also requested that the rehearing be conducted by the Precedential Opinion Panel. Ex. 3003. The Precedential Opinion Panel denied that request and directed us to consider Patent Owner's rehearing request. Paper 81, 3. The Precedential Opinion Panel directed us, "in [our] consideration on rehearing, to clearly identify whether the Voswinckel JESC and Voswinckel JAHA references qualify as prior art" and specified that "[s]uch analysis shall clarify whether the relied upon research aids were available prior to the critical date and whether the Voswinckel JESC and Voswinckel JAHA references were publicly accessible by way of their presentation and/or inclusion in distributed materials, such as at a conference or library." *Id.*

C. Standard of Review

A request for rehearing of an institution decision is reviewed under the abuse of discretion standard. 37 C.F.R. § 42.71(c). "The burden of showing a decision should be modified lies with the party challenging the decision." 37 C.F.R. § 42.71(d). "The request must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, reply, or a sur-reply." *Id.* An abuse of discretion may be found where a decision "(1) is clearly unreasonable, arbitrary, or fanciful; (2) is based on an erroneous conclusion of law; (3) rests on clearly erroneous fact findings; or (4) involves a record that contains no evidence on which the Board could rationally base its decision." *Redline Detection, LLC v. Star Envirotech, Inc.*, 811 F.3d 435, 442 (Fed. Cir. 2015) (quoting *Abrutyn v. Giovanniello*, 15 F.3d 1048, 1050–51 (Fed. Cir. 1994) (citation omitted)).

D. We Overlooked Patent Owner's Argument

Patent Owner is correct that its argument that the Ghofrani and Sulica research aids were dated after May 15, 2005, appeared in the Sur-Reply. Sur-Reply 9–11. Patent Owner also is correct that we overlooked this argument in relying on these research aids as supporting that Petitioner had established that Voswinckel JESC and Voswinckel JAHA were prior art to the '793 patent. Final Dec. 11–12; Paper 81, 2 ("the Board's analysis did not consider whether the research aids themselves were available prior to the critical date").

E. Reconsideration of the Record Shows that the Research Aids Did Not Establish the Prior-Art Status of Voswinckel JESC and Voswinckel JAHA

Petitioner argued that Voswinckel JESC and Voswinckel JAHA were "prior art to the '793 Patent under at least 35 U.S.C. § 102(b)." Pet. 22, 24. In the Final Written Decision, we determined that Petitioner had shown that these references were prior art based on the existence of research aids. Final Dec. 10–12. As noted above, that determination overlooked Patent Owner's argument that the research aids themselves were published too late for their mention of Voswinckel JESC and Voswinckel JAHA to render those references prior art under § 102(b). We now consider that argument.

To qualify as prior art under § 102(b), a reference must have been publicly accessible "more than one year prior to the date of application for patent in the United States." 35 U.S.C. § 102(b) (2006). Here, the parties agree that the application that ultimately led to the issuance of the '793 patent was filed May 15, 2006. Pet. 12; PO Resp. 5. Thus, to qualify as § 102(b) prior art, Voswinckel JESC and Voswinckel JAHA must have been publicly accessible before May 15, 2005.

Petitioner argues that Voswinckel JESC "was cited in the June 2005 Ghofrani article in the journal *Herz* . . . , an article that was publicly accessible." Reply 3 (citing Ex. 1010, 298, 301). Patent Owner argues that "Ghofrani bears a July 2005 date-stamp." Sur-Reply 9 (citing Ex. 1121, 1). Petitioner does not explain its characterization of Ghofrani as a "June 2005" article. The pages of Ghofrani cited by Petitioner do not indicate a June 2005 publication date.

Ex. 1010, 298, 301. The same article appears, however, as Exhibit 1121, which bears a date of July 7, 2005. *Compare* Ex. 1010, *with* Ex. 1121. Accordingly, Patent Owner's characterization of Ghofrani as having been published in July 2005 is better supported by the evidence of record than is Petitioner's characterization of Ghofrani as having been published in June 2005. Even if the evidence of record supported Petitioner's June 2005 publication date, that date is still later than May 15, 2005, so the citation of Voswinckel JESC in Ghofrani does not show that Voswinckel JESC was prior art under § 102(b).

Petitioner argues that Voswinckel JAHA "was cited by a March 2005 article authored by Roxana Sulica et al. in the *Expert Review of Cardiovascular Therapy*." Reply 7 (citing Ex. 1104, 359). Patent Owner argues that the Sulica article "shows only the year 2005." Sur-Reply 9 (citing Ex. 1104, 347). We agree with Patent Owner. The Sulica article bears a 2005 copyright date but otherwise does not indicate when it was published. Ex. 1104, 347. The 2005 copyright date does not support a finding that the Sulica article was published before May 15, 2005, so the citation of Voswinckel JAHA in the Sulica article does not show that Voswinckel JAHA was prior art under § 102(b).

F. Reexamination of the Record Shows that Voswinckel JESC and Voswinckel JAHA Were Prior Art to the '793 Patent Due to Distribution at Conferences

The Precedential Opinion Panel directed us, "in [our] consideration on rehearing, to clearly identify whether the Voswinckel JESC and Voswinckel JAHA references qualify as prior art" and specified that "[s]uch analysis shall clarify . . . whether the Voswinckel JESC and Voswinckel JAHA references

were publicly accessible by way of their presentation and/or inclusion in distributed materials, such as at a conference or library." Paper 81, 3. Accordingly, we consider below whether the evidence of record establishes the prior-art status of Voswinckel JESC and Voswinckel JAHA due to presentation and/or inclusion in distributed materials. We answer this question in the affirmative.

"Because there are many ways in which a reference may be disseminated to the interested public, 'public accessibility' has been called the touch-stone in determining whether a reference constitutes a 'printed publication.'" *Jazz Pharm., Inc. v. Amneal Pharm., LLC*, 895 F.3d 1347, 1356 (Fed. Cir. 2018) (quoting *In re Hall*, 781 F.2d 897, 898–99 (Fed. Cir. 1986)). A reference is considered publicly accessible if it was "disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it." *Id.* at 1355–56 (citing *In re Wyer*, 655 F.2d 221, 226 (CCPA 1981)). Under at least some circumstances, a reference may be a printed publication under § 102(b) if it was "displayed to the public," even if it "was not later indexed in any database, catalog, or library." *In re Klopfenstein*, 380 F.3d 1345, 1350 (Fed. Cir. 2004). There are several factors relating to whether such a display is sufficient to constitute a printed publication, including "the length of time the display was exhibited, the expertise of the target audience, the existence (or lack thereof) of reasonable expectations that the material displayed would not be copied, and the simplicity or ease with which the material displayed could have been copied." *Id.* In addition, distribution of a reference at a professional conference may, under at least some circumstances, constitute sufficient dissemina-

tion to show public accessibility. *Nobel Biocare Services AG v. Instradent USA, Inc.*, 903 F.3d 1365, 1375–80 (Fed. Cir. 2018); *Medtronic, Inc. v. Barry*, 891 F.3d 1368, 1380–83 (Fed. Cir. 2018).

1. Voswinckel JESC Was Sufficiently Distributed at a Conference to be Publicly Accessible as of the Conference Date

A reference may be "[a] printed publication ' . . . if it was sufficiently disseminated at the time of its publication.'" *Medtronic*, 891 F.3d at 1381 (quoting *Suffolk Techs., LLC v. AOL Inc.*, 752 F.3d 1358, 1365 (Fed. Cir. 2014)). Several factors are relevant to the determination of whether distribution of a reference at a conference constitutes such sufficient dissemination. *Id.* at 1381–82. These include "the size and nature of the meetings and whether they are open to people interested in the subject matter of the material disclosed," as well as "whether there is an expectation of confidentiality between the distributor and the recipients of the materials." *Id.* at 1382. "The expertise of the target audience can [also] be a factor in determining public accessibility." *Id.* To the extent that these factors are addressed via testimonial evidence, corroboration of that evidence may be necessary. *Nobel Biocare*, 903 F.3d at 1377–78. "Corroborating evidence may include documentary or testimonial evidence," and "[c]ircumstantial evidence can be sufficient corroboration." *Id.* (citing *TransWeb, LLC v. 3M Innovative Props. Co.*, 812 F.3d 1295, 1301 (Fed. Cir. 2016)).

Voswinckel JESC is an abstract contained in "Volume 25 Abstract Supplement August/September 2004" of "European Heart Journal," with a subtitle indicating that the journal is the "Journal of the European Society of Cardiology" and that the

supplement relates to "ESC Congress 2004," held "28 August – 1 September" in "Munich, Germany." Ex. 1007, 1; *see also* Ex. 1089, 1. The Table of Contents organizes abstracts into categories, including "Epidemiology and treatment of pulmonary arterial hypertension," with each category associated with an entry corresponding to a day of the conference, such as "Day 2—Sunday 29 August 2004." *Id.* at 2. Each of these categories points to a page or pages in the supplement, with those pages containing abstracts that report the "Background," "Methods," "Results," and "Conclusion" of studies. *Id.* at 7.

The conference with which Voswinckel JESC is associated "is the largest medical congress in Europe and among the top three cardiology meetings in the world," and "it has become an established forum for the exchange of science as much as education." Ex. 1105, 19. Attendees of the conference include "basic scientists, nurses and allied professionals working in the field of cardiovascular care of patients." *Id.* At the 2004 conference, there were "24,527 attendees," including "18,413 professionals, 4,715 exhibitors, 636 journalists and 763 accompanying persons." *Id.* Both Petitioner's declarant, Dr. Nicholas Hill, and Patent Owner's declarant, Dr. Aaron Waxman, testify that anyone who paid to attend the ESC Congress 2004 would have received a copy of the abstract book from which Voswinckel JESC is excerpted, either at the meeting itself or as a distribution before the meeting. Ex. 1106 ¶ 28; Ex. 1108, 105:16–108:1.

Thus, the evidence of record shows that Voswinckel JESC was distributed to more than twenty thousand people before or at the time of the ESC Congress 2004 in late August and early September of 2004. Those twenty thousand recipients included both highly

skilled professionals, including scientists, nurses, and other clinicians, as well as journalists and those who accompanied the professionals and the journalists. That the recipients included journalists and "accompanying persons" suggests very strongly that there was no expectation that the contents of Voswinckel JESC would be kept confidential. Moreover, Drs. Hill and Waxman corroborate one another's testimony, and their testimony is further corroborated by the contents of both Voswinckel JESC itself and Exhibit 1105. The distribution of Voswinckel JESC to over twenty thousand recipients, including thousands of experts in the field of cardiology, with no expectation of confidentiality, establishes that Voswinckel JESC was a printed publication as of the date of the conference at which that distribution occurred. Because that conference occurred in August and September 2004, more than one year before the May 15, 2006 application date of the '793 patent, Voswinckel JESC was a printed publication early enough to qualify as prior art under 35 U.S.C. § 102(b).

2. Voswinckel JAHA Was Sufficiently Distributed at a Conference to be Publicly Accessible as of the Conference Date

Like Voswinckel JESC, Voswinckel JAHA is associated with a professional conference. Ex. 1008. It is an abstract that has been extracted from a document headed "Supplement to Circulation," subtitled "Journal of the American Heart Association" and "Abstracts from Scientific Sessions 2004," indicating that those sessions occurred "November 7–10." *Id.* at 1. The abstract in question appears in a section titled "Pulmonary Arterial Hypertension: New Therapies," subtitled "Subspecialty: Integrative Biology" and indicating that the session occurred on

"Wednesday" in "Hall I2" of the "Ernest N Morial Convention Center." *Id.* at 3. We take official notice that the range of dates from November 7, 2004, to November 10, 2004, includes Wednesday, November 10, 2004.

Both Dr. Hill and Dr. Waxman agree that attendance at the Scientific Sessions 2004 conference was large. Ex. 1106 ¶ 22 ("a [person of ordinary skill in the art] would have attended the Scientific Sessions 2004 Conference, as it is one of the principal conferences on the circulatory system and diseases and conditions affecting circulation"); Ex. 1108, 116:4–21 (testifying that attendance at Scientific Sessions 2004 was likely larger than the 18,000 professionals who attended ESC Congress 2004). Dr. Hill testifies that the conference was "attended by physicians and researchers working on and studying the cardiovascular system, including pulmonary circulation." *Id.* Both Dr. Hill and Dr. Waxman also agree that a copy of the abstract book from which Voswinckel JAHA is excerpted would have been provided to all attendees at Scientific Sessions 2004. Ex. 1106 ¶ 23; Ex. 1108, 108:3–20. We have not been directed to any evidence of record indicating there was any expectation of confidentiality. The distribution of thousands of copies of Voswinckel JAHA at the conference is strong evidence that Voswinckel JAHA was a printed publication as of the date of the conference. Because that conference occurred in November 2004, more than one year before the May 15, 2006 application date of the '793 patent, Voswinckel JAHA was a printed publication early enough to qualify as prior art under 35 U.S.C. § 102(b).

3. Conclusion

As instructed by the Precedential Opinion Panel, we have considered "whether the Voswinckel JESC and Voswinckel JAHA references qualify as prior art" and in particular "whether the Voswinckel JESC and Voswinckel JAHA references were publicly accessible by way of their presentation and/or inclusion in distributed materials, such as at a conference." Paper 81,3. As discussed above, we find that both references were distributed sufficiently at professional conferences to be publicly accessible at the time of those conferences. By virtue of this public accessibility, both Voswinckel JESC and Voswinckel JAHA were printed publications early enough to qualify as prior art under 35 U.S.C. § 102(b).

G. Asserted Obviousness over '212 Patent, Voswinckel JESC, and Voswinckel JAHA

Petitioner argues that claims 1–8 would have been obvious over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA. Pet. 30–46. As discussed above, Petitioner has shown by a preponderance of the evidence that both Voswinckel JESC or Voswinckel JAHA qualify as prior art. Accordingly, we do not disturb the obviousness analysis in the Final Written Decision, which relies on the prior-art status of Voswinckel JESC and Voswinckel JAHA. Final Dec. 12–35.

H. Remaining Grounds

Petitioner argues that claims 1–8 would have been obvious over the combination of the '212 patent and Voswinckel JESC. Pet. 46–50. We do not disturb the determination in the Final Written Decision that we need not reach this ground "[b]ecause Petitioner has shown by a preponderance of the evidence that all of

the challenged claims would have been obvious over the similar combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA." Final Dec. 36.

Petitioner argues that claim 1 was anticipated by Ghofrani; that claims 1, 3, and 8 would have been obvious over the combination of Voswinckel JAHA and Ghofrani; that claims 1 and 3 were anticipated by Voswinckel 2006; and that claims 2 and 4–8 would have been obvious over the combination of Voswinckel 2006 and the '212 patent. Pet. 50–64. These grounds fail for the reasons discussed in the Final Written Decision. Final Dec. 36–41.

CONCLUSION[1]

For the reasons discussed above, Patent Owner has shown that we overlooked its argument regarding the date of availability of the research aids that Petitioner argued showed that Voswinckel JESC and Voswinckel JAHA qualified as prior art. A proper consideration of that argument shows that the research aids do not establish the prior-art status of Voswinckel JESC and Voswinckel JAHA, but there is no change to the outcome with respect to Petitioner's asserted grounds of unpatentability, because the

[1] 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).

distribution of Voswinckel JESC and Voswinckel JAHA at professional conferences proves the prior-art status of those references. Accordingly, we deny Patent Owner's request for rehearing.

When all arguments are properly considered, Petitioner has shown by a preponderance of the evidence that claims 1–8 of the '793 patent are unpatentable.

Outcome of Decision on Rehearing:

Claims	35 U.S.C. §	Reference(s)/ Basis	Denied	Granted
1–8	103(a)	'212 patent, Voswinckel JESC, Voswinckel JAHA	1–8	
Overall Outcome			1–8	

Final Outcome of Final Written Decision after Rehearing:

Claims	35 U.S.C. §	Reference(s) / Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1–8	103(a)	'212 patent, Voswinckel JESC, Voswinckel JAHA	1–8	
1–8	103(a)	'212 patent, Voswinckel JESC[2]		
1	102(a)	Ghofrani		1
1, 3, 8	103(a)	Voswinckel JAHA, Ghofrani		1, 3, 8
1, 3	102(a)	Voswinckel 2006		1, 3
2, 4–8	103(a)	Voswinckel 2006, '212 patent		2, 4–8
Overall Outcome			1–8	

[2] Neither the Final Written Decision nor this Rehearing Decision reaches this ground because Petitioner has proven all challenged claims are unpatentable based on obviousness over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA.

ORDER

It is hereby

ORDERED that Patent Owner's Request for Rehearing is denied;

FURTHER ORDERED that the determination in the Final Written Decision that the research aids relied on by Petitioner show the prior-art status of Voswinckel JESC and Voswinckel JAHA is overturned and replaced with the determination in the present decision that the distribution of Voswinckel JESC and Voswinckel JAHA at professional conferences establishes the prior-art status of those references;

FURTHER ORDERED that, based on the preponderance of the evidence, claims 1–8 of the '793 patent have been shown to be unpatentable;

FURTHER ORDERED that all other rulings in the Final Written Decision remain undisturbed; and

FURTHER ORDERED that parties to this proceeding seeking judicial review of this Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

For PETITIONER:

Ivor R. Elrifi
Erik B. Milch
Deepa Kannappan
Sanya Sukduang
Lauren Krickl
Douglas Cheek
Jonathan Davies
COOLEY LLP

ielrifi@cooley.com
emilch@cooley.com
dkannappan@cooley.com
ssukduang@cooley.com
lkrickl@cooley.com
dcheek@cooley.com
jdavies@cooley.com

For PATENT OWNER:

Stephen B. Maebius
George Quillin
Jason N. Mock
Michael Houston
FOLEY & LARDNER LLP
smaebius@foley.com
gquillin@foley.com
jmock@foley.com
mhouston@foley.com

Shaun R. Snader
UNITED THERAPEUTICS CORP.
ssnader@unither.com

Douglas Carsten
April E. Weisbruch
Judy Mohr
Jiaxiao Zhang
Mandy Kim
Arthur Dykhuis
Amy Mahan
MCDERMOTT WILL & EMERY LLP
dcarsten@mwe.com
aweisbruch@mwe.com
jmohr@mwe.com
jazhang@mwe.com
mhkim@mwe.com
adykhuis@mwe.com
amahan@mwe.com

APPENDIX G

35 U.S.C. § 311

Inter partes review

(a) In General.—Subject to the provisions of this chapter, a person who is not the owner of a patent may file with the Office a petition to institute an inter partes review of the patent. The Director shall establish, by regulation, fees to be paid by the person requesting the review, in such amounts as the Director determines to be reasonable, considering the aggregate costs of the review.

(b) Scope.—A petitioner in an inter partes review may request to cancel as unpatentable 1 or more claims of a patent only on a ground that could be raised under section 102 or 103 and only on the basis of prior art consisting of patents or printed publications.

(c) Filing Deadline.—A petition for inter partes review shall be filed after the later of either—

> **(1)** the date that is 9 months after the grant of a patent; or
>
> **(2)** if a post-grant review is instituted under chapter 32, the date of the termination of such post-grant review.

* * * *

35 U.S.C. § 312:

Petitions

(a) Requirements of Petition.—A petition filed under section 311 may be considered only if—

> **(1)** the petition is accompanied by payment of the fee established by the Director under section 311;

(2) the petition identifies all real parties in interest;

(3) the petition identifies, in writing and with particularity, each claim challenged, the grounds on which the challenge to each claim is based, and the evidence that supports the grounds for the challenge to each claim, including—

(A) copies of patents and printed publications that the petitioner relies upon in support of the petition; and

(B) affidavits or declarations of supporting evidence and opinions, if the petitioner relies on expert opinions;

(4) the petition provides such other information as the Director may require by regulation; and

(5) the petitioner provides copies of any of the documents required under paragraphs (2), (3), and (4) to the patent owner or, if applicable, the designated representative of the patent owner.

(b) Public Availability.—As soon as practicable after the receipt of a petition under section 311, the Director shall make the petition available to the public.

* * * *

35 U.S.C. § 313:

Preliminary response to petition

If an inter partes review petition is filed under section 311, the patent owner shall have the right to file a preliminary response to the petition, within a time period set by the Director, that sets forth reasons why no inter partes review should be instituted based upon

the failure of the petition to meet any requirement of this chapter.

* * * *

35 U.S.C. § 314:

Institution of inter partes review

(a) Threshold.—The Director may not authorize an inter partes review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.

(b) Timing.—The Director shall determine whether to institute an inter partes review under this chapter pursuant to a petition filed under section 311 within 3 months after—

> **(1)** receiving a preliminary response to the petition under section 313; or
>
> **(2)** if no such preliminary response is filed, the last date on which such response may be filed.

(c) Notice.—The Director shall notify the petitioner and patent owner, in writing, of the Director's determination under subsection (a), and shall make such notice available to the public as soon as is practicable. Such notice shall include the date on which the review shall commence.

(d) No Appeal.—The determination by the Director whether to institute an inter partes review under this section shall be final and nonappealable.

* * * *

35 U.S.C. § 315:

Relation to other proceedings or actions

(a) Infringer's Civil Action.—

(1) Inter partes review barred by civil action.—An inter partes review may not be instituted if, before the date on which the petition for such a review is filed, the petitioner or real party in interest filed a civil action challenging the validity of a claim of the patent.

(2) Stay of civil action.—If the petitioner or real party in interest files a civil action challenging the validity of a claim of the patent on or after the date on which the petitioner files a petition for inter partes review of the patent, that civil action shall be automatically stayed until either—

(A) the patent owner moves the court to lift the stay;

(B) the patent owner files a civil action or counterclaim alleging that the petitioner or real party in interest has infringed the patent; or

(C) the petitioner or real party in interest moves the court to dismiss the civil action.

(3) Treatment of counterclaim.—A counterclaim challenging the validity of a claim of a patent does not constitute a civil action challenging the validity of a claim of a patent for purposes of this subsection.

(b) Patent Owner's Action.—An inter partes review may not be instituted if the petition requesting the

proceeding is filed more than 1 year after the date on which the petitioner, real party in interest, or privy of the petitioner is served with a complaint alleging infringement of the patent. The time limitation set forth in the preceding sentence shall not apply to a request for joinder under subsection (c).

(c) Joinder.—If the Director institutes an inter partes review, the Director, in his or her discretion, may join as a party to that inter partes review any person who properly files a petition under section 311 that the Director, after receiving a preliminary response under section 313 or the expiration of the time for filing such a response, determines warrants the institution of an inter partes review under section 314.

(d) Multiple Proceedings.—Notwithstanding sections 135(a), 251, and 252, and chapter 30, during the pendency of an inter partes review, if another proceeding or matter involving the patent is before the Office, the Director may determine the manner in which the inter partes review or other proceeding or matter may proceed, including providing for stay, transfer, consolidation, or termination of any such matter or proceeding.

(e) Estoppel.—

> **(1) Proceedings before the Office.**—The petitioner in an inter partes review of a claim in a patent under this chapter that results in a final written decision under section 318(a), or the real party in interest or privy of the petitioner, may not request or maintain a proceeding before the Office with respect to that claim on any ground that the petitioner raised

or reasonably could have raised during that inter partes review.

(2) Civil actions and other proceedings.—The petitioner in an inter partes review of a claim in a patent under this chapter that results in a final written decision under section 318(a), or the real party in interest or privy of the petitioner, may not assert either in a civil action arising in whole or in part under section 1338 of title 28 or in a proceeding before the International Trade Commission under section 337 of the Tariff Act of 1930 that the claim is invalid on any ground that the petitioner raised or reasonably could have raised during that inter partes review.

* * * *

35 U.S.C. § 316:

Conduct of inter partes review

(a) Regulations.—The Director shall prescribe regulations—

(1) providing that the file of any proceeding under this chapter shall be made available to the public, except that any petition or document filed with the intent that it be sealed shall, if accompanied by a motion to seal, be treated as sealed pending the outcome of the ruling on the motion;

(2) setting forth the standards for the showing of sufficient grounds to institute a review under section 314(a);

(3) establishing procedures for the submission of supplemental information after the petition is filed;

(4) establishing and governing inter partes review under this chapter and the relationship of such review to other proceedings under this title;

(5) setting forth standards and procedures for discovery of relevant evidence, including that such discovery shall be limited to—

(A) the deposition of witnesses submitting affidavits or declarations; and

(B) what is otherwise necessary in the interest of justice;

(6) prescribing sanctions for abuse of discovery, abuse of process, or any other improper use of the proceeding, such as to harass or to cause unnecessary delay or an unnecessary increase in the cost of the proceeding;

(7) providing for protective orders governing the exchange and submission of confidential information;

(8) providing for the filing by the patent owner of a response to the petition under section 313 after an inter partes review has been instituted, and requiring that the patent owner file with such response, through affidavits or declarations, any additional factual evidence and expert opinions on which the patent owner relies in support of the response;

(9) setting forth standards and procedures for allowing the patent owner to move to amend the patent under subsection (d) to cancel a challenged claim or propose a reasonable number of substitute claims, and ensuring that any information submitted by the patent owner

in support of any amendment entered under subsection (d) is made available to the public as part of the prosecution history of the patent;

(10) providing either party with the right to an oral hearing as part of the proceeding;

(11) requiring that the final determination in an inter partes review be issued not later than 1 year after the date on which the Director notices the institution of a review under this chapter, except that the Director may, for good cause shown, extend the 1-year period by not more than 6 months, and may adjust the time periods in this paragraph in the case of joinder under section 315(c);

(12) setting a time period for requesting joinder under section 315(c); and

(13) providing the petitioner with at least 1 opportunity to file written comments within a time period established by the Director.

(b) Considerations.—In prescribing regulations under this section, the Director shall consider the effect of any such regulation on the economy, the integrity of the patent system, the efficient administration of the Office, and the ability of the Office to timely complete proceedings instituted under this chapter.

(c) Patent Trial and Appeal Board.—The Patent Trial and Appeal Board shall, in accordance with section 6, conduct each inter partes review instituted under this chapter.

(d) Amendment of the Patent.—

(1) In general.—During an inter partes review instituted under this chapter, the patent owner

may file 1 motion to amend the patent in 1 or more of the following ways:

(A) Cancel any challenged patent claim.

(B) For each challenged claim, propose a reasonable number of substitute claims.

(2) Additional motions.—Additional motions to amend may be permitted upon the joint request of the petitioner and the patent owner to materially advance the settlement of a proceeding under section 317, or as permitted by regulations prescribed by the Director.

(3) Scope of claims.—An amendment under this subsection may not enlarge the scope of the claims of the patent or introduce new matter.

(e) Evidentiary Standards.—In an inter partes review instituted under this chapter, the petitioner shall have the burden of proving a proposition of unpatentability by a preponderance of the evidence.

* * * *

35 U.S.C. § 317:

Settlement

(a) In General.—An inter partes review instituted under this chapter shall be terminated with respect to any petitioner upon the joint request of the petitioner and the patent owner, unless the Office has decided the merits of the proceeding before the request for termination is filed. If the inter partes review is terminated with respect to a petitioner under this section, no estoppel under section 315(e) shall attach to the petitioner, or to the real party in interest or privy of the petitioner, on the basis of that petitioner's institution of that inter partes review. If no petitioner

remains in the inter partes review, the Office may terminate the review or proceed to a final written decision under section 318(a).

(b) Agreements in Writing.—Any agreement or understanding between the patent owner and a petitioner, including any collateral agreements referred to in such agreement or understanding, made in connection with, or in contemplation of, the termination of an inter partes review under this section shall be in writing and a true copy of such agreement or understanding shall be filed in the Office before the termination of the inter partes review as between the parties. At the request of a party to the proceeding, the agreement or understanding shall be treated as business confidential information, shall be kept separate from the file of the involved patents, and shall be made available only to Federal Government agencies on written request, or to any person on a showing of good cause.

* * * *

35 U.S.C. § 318:

Decision of the Board

(a) Final Written Decision.—If an inter partes review is instituted and not dismissed under this chapter, the Patent Trial and Appeal Board shall issue a final written decision with respect to the patentability of any patent claim challenged by the petitioner and any new claim added under section 316(d).

(b) Certificate.—If the Patent Trial and Appeal Board issues a final written decision under subsection (a) and the time for appeal has expired or any appeal has terminated, the Director shall issue and publish a

certificate canceling any claim of the patent finally determined to be unpatentable, confirming any claim of the patent determined to be patentable, and incorporating in the patent by operation of the certificate any new or amended claim determined to be patentable.

(c) Intervening Rights.—Any proposed amended or new claim determined to be patentable and incorporated into a patent following an inter partes review under this chapter shall have the same effect as that specified in section 252 for reissued patents on the right of any person who made, purchased, or used within the United States, or imported into the United States, anything patented by such proposed amended or new claim, or who made substantial preparation therefor, before the issuance of a certificate under subsection (b).

(d) Data on Length of Review.—The Office shall make available to the public data describing the length of time between the institution of, and the issuance of a final written decision under subsection (a) for, each inter partes review.

* * * *

35 U.S.C. § 319:

Appeal

A party dissatisfied with the final written decision of the Patent Trial and Appeal Board under section 318(a) may appeal the decision pursuant to sections 141 through 144. Any party to the inter partes review shall have the right to be a party to the appeal.