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Paper 20
Date: May 12, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INCYTE CORPORATION,
Petitioner,

v.

CONCERT PHARMACEUTICALS, INC.,
Patent Owner.

PGR2021-00006
Patent 10,561,659 B2

Before CHRISTOPHER G. PAULRAJ, ROBERT A. POLLOCK, and DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

NEWMAN, *Administrative Patent Judge*.

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

I. INTRODUCTION

A. Background

On October 28, 2020, Incyte Corporation ("Petitioner") filed a Petition (Paper 1, "Pet.") requesting a post-grant review of claims 1–21 (the "challenged claims") of U.S. Patent No. 10,561,659 B2 (Ex. 1001, "the '659 patent"). Concert Pharmaceuticals, Inc., ("Patent Owner") filed a Preliminary Response (Paper 11, "Prelim. Resp."). *See* 35 U.S.C. §§ 321–329 (2018). With authorization (*see* Paper 16), Petitioner filed a Reply to Patent Owner's Preliminary Response (Paper 17, "Reply") and Patent Owner filed a Preliminary Sur-Reply (Paper 19, "Prelim. Sur-Reply").

We have the authority and discretion to determine whether to institute a post grant review. 35 U.S.C. § 324; 37 C.F.R. § 42.4(a)(2020). We may not institute a post-grant review unless "the information presented in the petition . . . , if such information is not rebutted, would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." 35 U.S.C. § 324(a). After considering the briefing and the evidence of record, we determine that Petitioner has demonstrated that it is more likely than not that at least one of the challenged claims is unpatentable. Accordingly, we institute a post-grant review of all challenged claims of the '659 patent, based on all of the grounds identified in the Petition. *See SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (interpreting the statute to require "a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition"). The following preliminary findings of fact and conclusions of law are made

for the sole purpose of determining whether to institute review. Any final decision will be based on the full trial record.

B. Real Parties-in-Interest

Petitioner identifies itself as the real party-in-interest for Petitioner. Pet. 91. Patent Owner identifies itself as the real party-in-interest for Patent Owner. Paper 5, 1.

C. Related Proceedings

Petitioner identifies pending U.S. Application No. 16/704,402, which claims the benefit of priority to U.S. Application No. 16/098,338. IPR2017-01256 against Patent Owner's U.S. Patent No. 9,249,149 is pending, as it was remanded in light of *Arthrex, Inc. v. Smith & Nephew, Inc.*, 941 F.3d 1320 (Fed. Cir. 2019), *cert. granted*, *Arthrex, Inc v. Smith & Nephew, Inc., et al.*, No. 19-1458, 2020 WL 6037208 (U.S. Oct. 13, 2020), and then stayed by the PTAB. *Id*. Patent Owner also identifies U.S. Patent Application No. 16/704,402 as currently pending before the United States Patent and Trademark Office. Paper 5, 1.

D. The '659 Patent (Ex. 1001)

The '659 patent is entitled "Treatment of Hair Loss Disorders with Deuterated JAK Inhibitors," and issued on February 18, 2020. Ex. 1001, at codes (54), (45). According to the '659 patent, many current medicines suffer from poor adsorption, distribution, metabolism, and/or excretion ("ADME") properties that limit their use for certain indications. *Id*. at 1:20–23. For example, rapid metabolism can cause drugs to be cleared too rapidly from the body, decreasing the drugs' efficacy in treating a disease. *Id*. at 1:29–32. Another ADME limitation is the formation of toxic or biologically reactive metabolites. *Id*. at 1:40–41.

The cytochrome P450 enzyme ("CYP") is typically responsible for the metabolism of drugs. *Id*. at 1:52–54. As such, the '659 patent identifies deuterium modification as a "potentially attractive strategy for improving a drug's metabolic properties." *Id*. at 2:7–8. Deuterium modification involves replacing one or more hydrogen atoms of a drug with deuterium atoms in an attempt to slow the CYP-mediated metabolism of a drug or to reduce the formation of undesirable metabolites. *Id*. at 2:8–12. Because deuterium forms stronger bonds with carbon than hydrogen, in certain cases, that stronger bond strength can positively impact the ADME properties of a drug, resulting in the potential for improved drug efficacy, safety, and/or tolerability. *Id*. at 2:13–19.

Ruxolitinib phosphate, a heteroaryl-substituted pyrrolo [2,3-d]pyrimidine, is an FDA-approved drug for treating patients with intermediate or high-risk myelofibrosis. *Id*. at 2:51–66. Ruxolitinib also has other potential applications, including the treatment of essential thrombocytopenia and is currently in clinical trials for the treatment of additional conditions. *Id*. at 2:66–3:5. Thus, according to the Specification, "[d]espite the beneficial activities of ruxolitinib, there is a continuing need for new compounds to treat the aforementioned diseases and conditions." *Id*. at 3:3–5.

The '659 patent discloses "a method for treating hair loss disorders that can be treated by compounds that modulate the activity of Janus Associated Kinase 1 (JAKl) and/or Janus Associated Kinase 2 (JAK2)." *Id.* at 3:43–46. The method comprises administering an effective amount of a deuterated compound (Compound I), or its pharmaceutically acceptable salt, once or twice a day, in specific dose ranges. *Id.* at 3:46–66. The method is

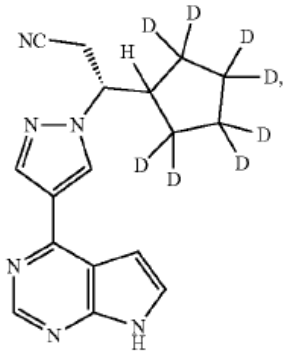
disclosed as for use in treating the hair loss disorder alopecia areata or for generally "inducing hair growth in a subject." *Id.* at 3:66–67; 4:18–20. The level of deuterium incorporation into the drug is disclosed as between 52.5% to upwards of 99.5%. *Id.* at 6:42–52.

E. Challenged Claims

Petitioner challenges claim 1–21 of the '659 patent. Claim 1 is illustrative and recites:

1. A method of treating a hair loss disorder in a mammalian subject, the method comprising administering to the subject 16 mg/day or 24 mg/day of a compound represented by the following structural formula:

Compound (I)



or a pharmaceutically acceptable salt thereof, wherein each position in Compound (I) designated specifically as deuterium has at least 95% incorporation of deuterium.

Ex. 1001, 24:30–53.

F. Prior Art and Asserted Grounds of Unpatentability

Petitioner argues that claims 1–21 of the '659 patent are unpatentable based on the following grounds[1]:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–21	103	Silverman[2], Xing[3], Ruxolitinib Prescribing Information[4]
1–21	103	Silverman, Christiano[5], Ni[6]

Pet. 2. Petitioner relies on the declarations of Dr. Steven Patterson, Ph.D., (Ex. 1007) and Dr. Jerry Shapiro, M.D. (Ex. 1009).

II. POST-GRANT ELIGIBILITY

The AIA's post-grant review provisions apply to patents that "contain[] or contained at any time . . . a claim to a claimed invention that has an effective filing date . . . that is on or after [March 16, 2013]." Leahy-Smith America Invents Act (AIA) §§ 3(n)(1), 6(f)(2)(A) (2011). In addition, "[a] petition for a post-grant review may only be filed not later than the date

[1] Ground 3 is no longer at issue in this case as Patent Owner filed a statutory disclaimer of claim 8 (*see* Ex. 2020). 37 C.F.R. § 42.207(e) ("No post-grant review will be instituted based on disclaimed claims.").
[2] Silverman et al., U.S. Patent 9,249,149 B2, issued February 16, 2016 (Ex. 1002, "Silverman").
[3] Xing et al., *Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition,* NAT. MED. 20(9):043–1049 (2014) (Ex. 1003, "Xing").
[4] Jakafi® (ruxolitinib) Prescribing Information, Physicians' Desk Reference 1281–1287 (69th ed. 2015) (Ex. 1004, "Ruxolitinib Prescribing Information").
[5] Christiano et al., U.S. Patent No. 9,198,911 B2, issued December 1, 2015 (Ex. 1005, "Christiano").
[6] Ni et al., U.S. Patent Pub. 2014/0135350 A1, published May 15, 2014 (Ex. 1006, "Ni").

that is 9 months after the date of the grant of the patent or of the issuance of a reissue patent (as the case may be)." 35 U.S.C. § 321(c) (2012); *see* 37 C.F.R. § 42.202(a).

Here, the '659 patent is eligible for post-grant review because the Petition was filed within nine months of the '659 patent's issue date and the earliest possible priority date of the '659 patent is after March 16, 2013 (the effective date for the first inventor to file provisions of the Leahy-Smith America Invents Act). Ex. 1001, code (45) (showing an issue date of February 18, 2020); *Id*. at 1:6–11. Patent Owner does not challenge this assertion. *See generally* Prelim. Resp.

III. ANALYSIS

A. Discretionary Denial Under 35 U.S.C. § 325(d)

Patent Owner argues we should exercise our discretion to deny institution of Grounds 1 and 2 under § 325(d). Prelim. Resp. 22–32. Patent Owner states that, "Incycte seeks to relitigate references and disclosures that the Patent Examiner already considered during prosecution." *Id*. at 22. Petitioner contends that Patent Owner "filed an RCE with a preliminary amendment and IDS listing several references." Pet. 19. However, Petitioner argues that because the Examiner "[e]rroneously" believed that the compound claimed in the '659 patent was novel, there was, "no discussion of these newly disclosed references or any rejections, [and] the Examiner allowed all the claims for the same reason as before." *Id*. at 1, 19. Patent Owner contends, "[t]he IDS identified three of Incyte's current references" and thus, "the art before the examiner and the art at issue in the petition are identical." Prelim. Resp. 24.

In evaluating arguments under § 325(d), we use a two-part framework to assess: (1) whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and (2) if either condition of first part of the framework is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential). In applying the two-part framework, we consider the non-exclusive factors set forth in *Becton, Dickinson and Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 (PTAB Dec. 15, 2017) (precedential in relevant part), which "provide useful insight into how to apply the framework" under § 325(d). *Advanced Bionics*, Paper 6 at 9. Those non-exclusive factors include:

> (a) the similarities and material differences between the asserted art and the prior art involved during examination;
>
> (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
>
> (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
>
> (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;
>
> (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and

> (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Becton, Paper 8 at 17–18. "If, after review of factors (a), (b), and (d), it is determined that the same or substantially the same art or arguments previously were presented to the Office, then factors (c), (e), and (f) relate to whether the petitioner has demonstrated a material error by the Office." *Advanced Bionics*, Paper 6 at 10.

1. Same or Substantially the Same Art or Arguments Previously Presented to the Office

We first consider whether Petitioner asserts the same or substantially the same art or arguments that previously were presented to the Office. *Advanced Bionics*, Paper 6 at 8. Patent Owner argues that "Silverman, Xing, and Christiano were directly before the examiner. And the Ruxolitinib Prescribing Information and Ni are not materially distinguishable from references that were before the examiner." Prelim. Resp. 24 (citing prosecution history at Ex. 1047 at 1521–1522).

With respect to Silverman, Xing, and Christiano, because these references were submitted on the Information Disclosure Statement during prosecution of the '659 patent, we agree with Patent Owner that the same prior art that Petitioner relies upon in the Petition was previously presented to the Office. Regarding Ruxuolitinib Prescribing Information and Ni, Patent Owner presented persuasive arguments that the references are not materially distinguishable from references that were before the examiner. *Id.* at 25–27 (citing Ex. 1047 at 619–626, 1409–1442). We thus determine that art substantially similar to Ruxolitinib Prescribing Information and Ni was previously presented to the Office.

Accordingly, we proceed to the second part of the *Advanced Bionics* framework and consider whether Petitioner has demonstrated that the Office erred in a manner material to the patentability of the challenged claims. *See Advanced Bionics*, Paper 6 at 10 ("[I]f the record of the Office's previous consideration of the art is not well developed or silent, then a petitioner may show the Office erred by overlooking something").

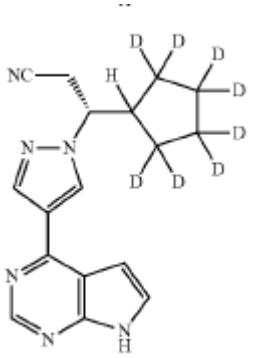
2. Whether Petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims

Petitioner argues that the Examiner, "[e]rroneously believing that 'Compound (I)' recited in the claims was novel," allowed the '659 patent without rejection. Pet. 1. Petitioner also contends, "[d]espite two interviews and an RCE, there is no evidence that Concert ever corrected the Examiner's misunderstanding." *Id*. Petitioner states the '659 patent covers "a formulation comprising Compound (I), an octa-deuterated analog of ruxolitinib, and method of using Compound (I) to treat hair loss disorders including alopecia areata." *Id*. Petitioner argues Compound (I) is not novel and was "disclosed with formulations and dosages in Concert's prior art U.S. Patent No. 9,249,149 to Silverman (EX1002 []) and was found obvious in IPR2017-01256 by the PTAB in 2019." *Id*.

Patent Owner contends that Petitioner offers no support for the assertion and simply declares it to be true that the Examiner erroneously believed that Compound (I) was novel. Prelim. Resp. 30. Patent Owner also contends, "there is no reason to believe that the examiner misunderstood the nature of compound (I)." *Id*.

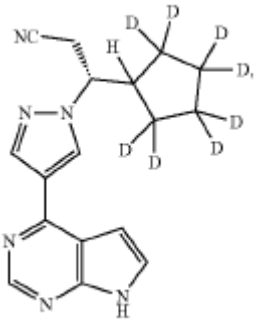
We are persuaded, on this preliminary record, that Silverman discloses key features of the subject matter of claim 1 that were overlooked

by the Examiner. As shown below, Silverman discloses Compound 111 (left), which is identical in structure to Compound I of the '659 patent claim 1 (right):



Silverman Compound 111

Ex. 1002, 37:29–42.



'659 Patent Compound I

Ex. 1001, 24:38–49.

Silverman further discloses use of Compound 111, in a form where each indicated "D" in the structure has at least a 95% incorporation of deuterium, and discloses use of the deuterated compound in methods of treating diseases and conditions that are beneficially treated by ruxolitinib. *See, e.g.*, Pet. 69–72. As such, we determine that the Examiner erred in a manner material to the patentability of the claims of the '659 patent by overlooking these disclosures of Silverman. *Id*.

Patent Owner argues that, rather than allow the '659 patent to issue, Patent Owner filed an RCE to, in part, submit references for the Examiner's consideration, and that the Examiner's modified statement in the Notice of Allowance highlights the Examiner's clear knowledge of Silverman's existence. Prelim. Resp. 30–31. Although the Examiner was undoubtedly aware of Silverman's existence, we are unpersuaded on this record that the Examiner was aware of the exact teachings of Silverman that Petitioner uses to challenge the '659 patent, namely the identity of Compound 111 and

Compound I of challenged claim 1. Even if the Examiner were aware of these particular teachings, as Patent Owner argues, we would still conclude that the Examiner materially erred. Accordingly, we decline to exercise our discretion to deny institution of post-grant review under 35 U.S.C. § 325(d).

B. Whether Silverman is Prior Art under 35 U.S.C. § 102(a)

Grounds 1 and 2 of the Petition allege obviousness using Silverman as the primary reference. Pet. 1–84. Patent Owner argues Silverman is not prior art under § 102 because it falls within exceptions set forth in § 102(b). Prelim. Resp. 12–21. Specifically, Patent Owner argues Silverman is not prior art because it satisfies the inventor disclosure exceptions in both 102(b)(1)(A) and 102(b)(1)(B) and because Silverman falls under the common-owner exception of 102(b)(2)(c). *Id.*

For the reasons that follow, we conclude that Patent Owner's evidence supporting its allegations that Silverman falls within the exceptions of § 102 is insufficiently persuasive on this record and needs to be tested at trial.

1. Legal Background

AIA 35 U.S.C. § 102(a) defines the prior art that will preclude the grant of a patent on a claimed invention and states:

> [a] person shall be entitled to a patent unless—
>
> (1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention; or
>
> (2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was

> effectively filed before the effective filing date of the claimed invention.

AIA 35 U.S.C. § 102(b) sets out exceptions to AIA 35 U.S.C. 102(a). Section 102(b)(1) provides two exceptions to § 102(a)(1) for disclosures made within one year of the effective filing date. Specifically, a disclosure made one year or less before the effective filing date of a claimed invention shall not be prior art under 35 U.S.C. 102(a)(1) with respect to the claimed invention if: (1) the disclosure was made by the inventor or joint inventor or by another who obtained the subject matter disclosed directly or indirectly from the inventor or a joint inventor; or (2) the subject matter disclosed had, before such disclosure, been publicly disclosed by the inventor or a joint inventor or by another who obtained the subject matter disclosed directly or indirectly from the inventor or a joint inventor.

With regard to establishing unpatentability, a petitioner retains the burden of persuasion throughout the proceeding. *See Dynamic Drinkware, LLC v. National Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). However, with regard to specific evidence supporting the unpatentability challenge, such as the priority date of a reference used to establish obviousness, a petitioner shifts the burden of production to dispute the effective priority date of a prior art reference to the patent owner by alleging obviousness based upon a reference that appears to be prior art on its face. *Id.* at 1379–1380 (burden of production satisfied by assertion of anticipation, shifting burden to patent owner). *See also Pfizer, Inc. v. Genentech, Inc.*, IPR2017-01488, Paper 27 at 13 (PTAB Dec. 1, 2017) (initial burden met where prior-art patents "predate the earliest possible priority date shown on the face of the" challenged patent).

2. AIA § 102(a)(1)

Patent Owner argues that Petitioner failed to sufficiently establish that Silverman is § 102 prior art. Prelim. Resp. 13–15. Petitioner alleges two counts of unpatentability, stating that Silverman, in combination with Xing and Ruxolitinib Prescribing Information in Ground 1 and Christiano and Ni in Ground 2, renders claims 1–21 obvious. Pet. 2–3. On its face, Silverman is § 102(a) prior art because Silverman issued on February 2, 2016 (Ex. 1002, code (45)), before the earliest filing date of any provisional application to which the '659 patent claims priority (Ex. 1001, code (60)). We find Petitioner has satisfied its initial burden of production of evidence on this issue. Accordingly, the burden of production shifts to Patent Owner to argue or produce evidence that Silverman is not prior art. *Dynamic Drinkware*, 800 F.3d at 1379.

a) Exceptions to § 102(a)(1)

Patent Owner contends Silverman is not prior art under 35 U.S.C. § 102(a)(1) because it falls within the exceptions found in § 102(b)(1)(A) and § 102(b)(1)(B). Prelim. Resp. 16–21.

(1) Exception under § 102(b)(1)(B)

Patent Owner alleges that Silverman falls under the § 102(b)(1)(B) exception because 1) Silverman issued on February 2, 2016, within one year of the May 4, 2016, filing date of the earliest priority application of the '659 patent; and 2) the material contained in Silverman was made public before Silverman was published by one of the '659 patent's inventors. Prelim. Resp. 16–17 (citing Ex. 1002, 1). Regarding the alleged public disclosure, Patent Owner contends that the key subject matter that Petitioner relies on in Silverman was disclosed by Vinita Uttamsingh, an inventor of the '659

patent. *Id*. at 17–18 (citing Ex. 1045, 390–417, Ex. 1001, 1). Dr. Uttamsingh submitted a declaration during the prosecution of Silverman that became public on August 27, 2015, with the publication of the application leading to the '659 patent. *Id*. at 17 (citing Ex. 1046, 1). According to Patent Owner, the Uttamsingh declaration disclosed the "key subject matter that underlies Incyte's reliance on Silverman," the structure of Compound (I), which Dr. Uttamsingh disclosed as "Compound 111" in Silverman. *Id*. at 17–18. (citing Ex. 1045, 404).

Petitioner contends that the exception under 35 U.S.C. § 102(b)(1)(B) does not apply because the Uttamsingh Declaration relied on by Patent Owner does not disclose the same subject matter as Silverman. Reply 3–4. Specifically, Petitioner contends that the Uttamsingh Declaration "only describes two *in vitro* assays comparing the metabolic stability of three compounds" and "[i]ts exhibits merely describe the assays and their numerical results . . . and include a copy of the ruxolitinib prescribing information" *Id*. at 4 (citing Ex. 1045, 390–407, 414–417). Petitioner contends:

> *Silverman* is a twenty-two-page patent relied upon for disclosing, *inter alia*, **[1]** Compound (I) is useful in "a method of treating a disease that is beneficially treated by ruxolitinib… comprising a step of administering to the subject an effective amount of a compound or a composition of this invention" (Pet., 14, 27, 29, 34–35); **[2]** motivation to replace ruxolitinib with Compound (I) (*id*., 37–38); **[3]** "an effective amount of… 10 mg to 25 mg, from 10 mg to 20 mg,… and from 5 to 10 mg" (*id*., 14, 27–28, 43–44); **[4]** dosing QD and BID (*id*., 14, 27, 52); **[5]** 97% deuterium incorporation (*id*., 13, 27–28, 30–31, 41–43); **[6]** Compound (I) synthesis (*id*., 58); and **[7]** phosphate salt (*id*., 13–14, 54–56). *Silverman*'s disclosure was also relied upon against disclaimed Claim 8, which Concert would have had no reason to

> disclaim if *Silverman* were not prior art. *See* Pet., 3, 87–91; POPR, 74; EX2020.

Id. (alterations in original). Petitioner also contends, "[i]ndeed, even if [the] *Uttamsingh Dec.* is an inventor-originated disclosure of Compound (I) generically, it is not a disclosure of the species of specific doses ranges and uses of 95% and 97% deuterium-incorporated Compound (I) disclosed by *Silverman*." *Id*. at 5.

In response to Petitioner's arguments, Patent Owner contends that the Uttamsingh Declaration clearly discloses Compound 111 of Silverman and plainly discloses the data from the described *in vitro* studies "showing Compound (I)/111's relative stability over ruxolitinib." Prelim. Sur-Reply 3. Patent Owner also contends Petitioner's "dismissal of the 2015 Uttamsingh Declaration on the ground that it is 'short' and 'only describes two *in vitro* assays comparing the metabolic stability of three compounds' does not undermine its significance as a prior inventor disclosure that disqualifies the relevant disclosures of Silverman as prior art." *Id*. at 5.

(2) Exception under § 102(b)(1)(A))

Patent Owner contends Silverman falls within the prior art exception under § 102(b)(1)(A) because Silverman was 1) issued on February 2, 2016, within one year of the May 4, 2016, filing date of the earliest priority application of the '659 patent; and 2) "the metabolic data in Silverman that support the disclosure and claims to deuterated compounds were obtained from Dr. Uttamsingh, a named inventor on the '659 patent." Prelim. Resp. 20. According to Patent Owner, the Silverman inventors obtained the data from the experiment disclosed in Example 4 of Silverman directly or indirectly from Dr. Uttamsingh, who was responsible for reporting data regarding improved metabolic stability, and that data supported Silverman's

claims to the genus of deuterated compounds disclosed to support patentability during the prosecution of Silverman. *Id*. (citing Ex. 2005 ¶¶ 5–7).

Petitioner contends that "the non-public disclosure of two *in vitro* experiments described in EX2005 ('*2021 Uttamsingh Dec*') is not the same as *Silverman*'s relied upon disclosure of, *inter alia*, motivation, methods of use, purity levels, and forms of administration for Compound (I)." Reply 6. Petitioner also argues that the Uttamsingh Declaration "does not provide the referenced 'PowerPoint Presentation' or even identify who (beyond 'my group') presented it to the *Silverman* inventors" thus, the Declaration is materially deficient and unsupported. *Id*. at 7 (citing Ex. 2005 ¶ 7; FITF[7], 11,081; MPEP § 717.01(a)(1) (9th ed. rev. 10.2019 June 2020)). Further, Petitioner contends, "[a]ny inference that the subject matter of *Silverman* was obtained from Dr. Uttamsingh should be rejected as it contradicts the *Silverman* inventors' oaths that they are the 'original joint inventor[s] of a claimed invention in the application.'" *Id*. (citing Ex. 1045, 92–96; FITF, 11,080; *Ex parte Kroger*, 219 U.S.P.Q. 370 (Bd. App. 1982)) (second alteration in original).

In response to Petitioner's arguments, Patent Owner contends, "[o]nce the Board sets aside the specific disclosures that Dr. Uttamsingh made to the Silverman inventors—i.e., disclosure of the metabolic assay data used in the patent specification—any remaining disclosures of Silverman are insufficient to support institution." Prelim. Sur-Reply 6. Patent Owner also

[7] Petitioner cites to 78 Fed. Reg. 11,059, 10,161, 10,067 (Examination Guidelines for Implementing the First Inventor To File Provisions of the Leahy-Smith America Invents Act) as "FITF." Reply *passim*.

contends that Petitioner's argument that any inference that the subject matter of Silverman was obtained from Dr. Uttamsingh should be rejected because it contradicts Silverman inventor's oath, fails as a matter of law because the disclosure "need not be an enabling disclosure such that the inventor would have to be a named inventor on the intervening disclosure." *Id*. (citing MPEP § 717.01(a)(1)).

3. Exception under AIA § 102(b)(2)(C)

Patent Owner additionally contends that Silverman is not prior art because it falls within the exception set forth in § 102(b)(2)(C). Prelim. Resp. 21; Prelim. Sur-Reply 7. Specifically, Patent Owner contends that Silverman is not prior art under 35 U.S.C. § 102(a)(2) because "[a]s of the effective filing date of the '659 patent, Concert was indisputably the owner of both Silverman and the application for the '659 patent." Prelim. Resp. 21 (citing Ex. 1002; Ex. 1047; Ex. 2010; Ex. 2011; Ex. 2012) (Fitzgerald declaration and patent cover sheets).

Petitioner contends that Patent Owner's assertion regarding co-ownership by Concert is easily dismissed because the '659 inventors did not assign their rights to Patent Owner until Oct. 16, 2017, such that the named inventors, not Patent Owner, owned the rights of inventorship reflected in the application for the '659 patent as of its effective filing date. Reply 2.

Patent Owner responds that the rights of inventorship reflected in the application resulting in the '659 patent were, nonetheless, subject to an obligation of assignment to Patent Owner and "the evidence demonstrates that Dr. Uttamsingh, a '659 patent inventor, was employed at Concert as of the effective filing date of the '659 patent." Prelim. Sur-Reply 7 (citing Ex. 2005 ¶ 3; Ex. 1045, 414, ¶ 1).

4. Conclusion

We conclude, on this record, that Patent Owner's evidence that the prior art exceptions under 35 U.S.C. § 102 apply to Silverman is insufficiently persuasive at this stage and needs to be tested at trial. We acknowledge that the Uttamsingh Declaration and the facts underlying it, if true, could demonstrate that Silverman is unavailable as prior art to the challenged claims under § 102(a). However, the following issues are germane to that determination, but insufficiently clear on the current record: (1) which inventors of the Silverman patent may have attended Dr. Uttamsingh's presentation, (2) whether any inventor did in fact learn the information alleged, and (3) whether Dr. Uttamsingh was bound at the time of the effective filing date of the claimed invention of '659 patent by an employment agreement obligating her to assign her rights in that invention to Concert. As a result, we encourage the parties to further develop at trial the record of facts underlying these issues.

C. Principles of Law of Obviousness

A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc*, 550 U.S. at 406. The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness, if any. *Graham v. John Deere Co*., 383 U.S. 1, 17–18 (1966). "Both the suggestion

and the expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Dow Chemical Co*., 837 F.2d 469, 473 (Fed. Cir. 1988).

In that regard, an obviousness analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418; *see In re Translogic Tech, Inc.*, 504 F.3d 1249, 1259 (Fed. Cir. 2007). In *KSR*, the Supreme Court also stated that an invention may be found obvious if trying a course of conduct would have been obvious to a POSA:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

550 U.S. at 421. "*KSR* affirmed the logical inverse of this statement by stating that § 103 bars patentability unless 'the improvement is more than the predictable use of prior art elements according to their established functions.'" *In re Kubin*, 561 F.3d 1351, 1359–60 (Fed. Cir. 2009) (citing *KSR*, 550 U.S. at 417).

We analyze the asserted grounds of unpatentability in accordance with the above-stated principles.

D. Person of Ordinary Skill in the Art

We consider the asserted grounds of unpatentability in view of the understanding of a person of ordinary skill in the art. *KSR*, 550 U.S. 398, 399 (2007) (stating that obviousness is determined against the backdrop of

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

Petitioner contends that a person of ordinary skill in the art would have had

> a Ph.D. in chemistry, pharmaceutical sciences, molecular biology, or a similar field, or an M.D. with similar background. A POSA would also have had at least several years of experience with drug design, drug development, clinical trials, or access to other individuals with that knowledge and experience. Likewise, a POSA would have had knowledge and experience in treating hair loss disorders, or access to a person with that knowledge and experience.

Pet. 19–20. Patent Owner does not dispute this definition for purpose of this post-grant review. Prelim. Resp. 12. Petitioner's proposed definition is consistent with the level of skill apparent in the cited prior art, and we adopt it for the purposes of this Decision.

E. Claim Construction

We construe claims using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 42.100. Therefore, we construe the challenged claims under the framework set forth in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc). Under this framework, claim terms are

given their ordinary and customary meaning, as would have been understood by a person of ordinary skill in the art ("POSA"), at the time of the invention, in light of the language of the claims, the specification, and the prosecution history of record. *Id.* Only those terms that are in controversy need be construed and only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Matal*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (citing *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

We have considered Petitioner's claim construction proposals (see Pet. 21–23), which are presently uncontested (Prelim. Resp. 12), and find that it is not necessary to expressly construe any claim term for purposes of rendering this Decision.

F. Petitioner's Expert Declaration

As a preliminary matter, Patent Owner argues that the Board should give little weight to the declarations provided by Petitioner's experts. Patent Owner argues:

> Dr. Patterson, Incycte's technical expert, does not have the requisite experience to offer opinions related to deuteration or JAK inhibitors. And Dr. Shapiro, Incyte's clinician, has taken positions in this matter that directly contradict his previous statements. Further, Incyte should not be permitted to incorporate by references large portions of Dr. Patterson's declaration without sufficient analysis of those sections.

Prelim. Resp. 70−74.

On the current record, we are not persuaded that Petitioner's expert declaration should be given little weight. "There is no requirement of a perfect match between the expert's experience and the relevant field." *SEB S.A. v. Montgomery Ward & Co.*, 594 F.3d 1360, 1373 (Fed. Cir. 2010). A

person must be "qualified in the pertinent art," not a person of ordinary skill in the art in order to testify as an expert under Federal Rule of Evidence 702. *Sundance, Inc. v. DeMonte Fabricating Ltd.*, 550 F.3d 1356, 1363–64 (Fed. Cir. 2008). Moreover, "[e]xpert opinion testimony is generally permitted where the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue." PTAB Consolidated Trial Practice Guide 34 (Nov. 2019), https://www.uspto.gov/TrialPracticeGuideConsolidated.

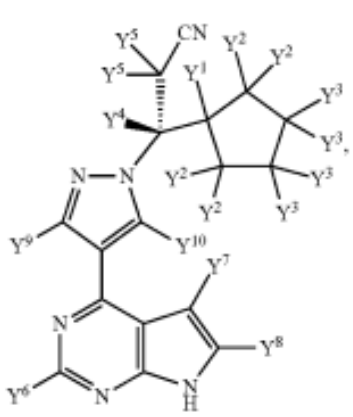
The panel finds the testimony of Dr. Patterson and Dr. Shapiro helpful to understand the relevant technology and evidence for the purposes of institution. Patent Owner is welcome to challenge Dr. Patterson's and Dr. Shapiro's testimony at trial, and the Board will assign their testimony appropriate weight based on the developed record.

G. Ground 1

1. Silverman (Ex. 1002)

Silverman discloses the compound of formula A or "a pharmaceutically acceptable salt thereof; pharmaceutical compositions comprising the compound; and methods of treating the indications disclosed herein." Ex. 1002, Abstract. Formula A is a "novel heteroaryl-substituted pyrrolo[2,3-d]pyrimidines, and pharmaceutically acceptable salts thereof." *Id.* at 3:25–27.

Formula A is reproduced below.



Formula A

or a pharmaceutically acceptable salt thereof, wherein:

Y^1 is selected from hydrogen and deuterium;

each Y^2 is independently selected from hydrogen and deuterium, provided that each Y^2 attached to a common carbon is the same;

each Y^3 is independently selected from hydrogen and deuterium, provided that each Y^3 attached to a common carbon is the same;

Y^4 is selected from hydrogen and deuterium;

each Y^5 is the same and is selected from hydrogen and deuterium; and

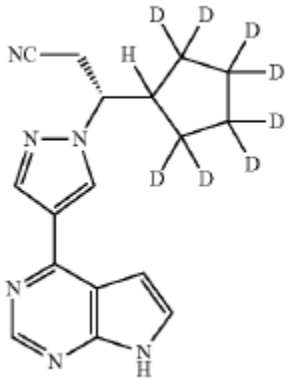
Y^6, Y^7, Y^8, Y^9, and Y^{10} are each independently selected from hydrogen and deuterium; provided that when Y^1 is hydrogen, each Y^2 and each Y^3 are hydrogen, Y^4 is hydrogen, and each of Y^6, Y^7, Y^8, Y^9, and Y^{10} is hydrogen, then each Y^5 is deuterium.

Id. at 6:7–42.

Formula A depicts a chemical structure or a compound obtained by deuterium substitution of the drug ruxolitinib phosphate, a heteroaryl-substituted pyrrolo[2,3-d]pyrimidines, which has been shown to inhibit Janus Associated Kinases (JAKs) and is an FDA-approved drug for treating patients with intermediate or high-risk myelofibrosis. *Id*. at 2:5–20; 2:53–65; 3:25–32. Ruxolitinib also has other potential applications, including the treatment of essential thrombocytopenia, psoriasis, and various forms of cancer. *Id*. at 3:3–6. Thus, "[d]espite the beneficial activities of ruxolitinib, there is a continuing need for new compounds to treat the aforementioned diseases and conditions." *Id*. at 3:19–21.

Deuterium substitution is performed to enhance the metabolic properties of a drug through enriching the isotopes by replacing one or more hydrogen atoms of the drug with deuterium atoms in an attempt to slow the CYP-mediated metabolism of a drug or to reduce the formation of undesirable metabolites. *Id*. at 2:6–10. Because deuterium forms stronger bonds with carbon than hydrogen, in certain cases, that stronger bond strength can positively impact the ADME properties of a drug, resulting in the potential for improved drug efficacy, safety, and/or tolerability. *Id*. at 2:11–15.

Silverman discloses multiple embodiments of Formula A, including Compound 111, which depicts deuterium substitutions at number of specific positions within the structure of Formula A:



Id. at 37:28–42. Embodiments of Formula A have "an isotopic enrichment factor for each designated deuterium atom" ranging between deuterium incorporation of 52.5% to at least 99.5%. *Id.* at 4:7–17.

Silverman discloses compositions including Formula A "and the use of such compositions in methods of treating diseases and conditions that are beneficially treated by administering an inhibitor of Janus-associated kinase with selectivity for subtypes 1 and 2 (JAK1/JAK2)." *Id.* at 3:27–32. Compositions can be made using a "pharmaceutically acceptable carrier" and may be "presented in unit dosage form, e.g., tables, sustained release capsules." *Id.* at 16:27; 17:4–5. Effective amounts can range from 5 g to 1 mg, and dosing can be daily or twice daily. *Id.* at 20:9–18. Silverman states that "guidance for selecting an effective dose can be determined by reference to the prescribing information for ruxolitinib." *Id.* at 20:25–27. Silverman also discloses that an embodiment can include a composition that "further comprises a second therapeutic agent . . . selected from any compound or therapeutic agent known to have or that demonstrates advantageous properties when administered with a compound having the same mechanism of action as ruxolitinib" and that the second agent is "useful in the treatment or prevention of a disease or condition selected from . . . alopecia areata." *Id.* at 19:42–50.

2. Xing (Ex. 1003)

Xing states "[a]lopecia areata (AA) is a common autoimmune disease that results from the damage of hair follicle by T cells." Ex. 1003, 1043. Xing further discloses that systemically administered pharmacological inhibitors of Janus Kinase family protein tyrosine kinases prevented the development of alopecia areata. *Id*. Xing states, "[n]otably three patients treated with oral ruxolitinib, an inhibitor of JAKl and JAK2, achieved near-complete hair regrowth within 5 months of treatment, suggesting the potential clinical utility of JAK inhibition in human AA." *Id*.

To test whether inhibition of signal pathways would be therapeutically effective *in vivo*, the authors systemically administered ruxolitinib and tofacitinib. *Id.* at 1048. Ruxolitinib was administered to patients orally, 20 mg twice daily. *Id.* The drugs were found to prevent the development of alopecia areata on areas where grafting had occurred, signifying a lack of inflammation development. *Id.* at 1048. Xing states "[t]he clinical response of a small number of patients with AA to treatment with the JAK1/2 inhibitor ruxolitinib suggests future clinical evaluation of this compound or other JAK protein tyrosine kinase inhibitors currently in clinical development is warranted in AA." *Id*. at 1048.

3. Ruxolitinib Prescribing Information (Ex. 1004)

Ruxolitinib Prescribing Information ("RPI"), an excerpt from the 2015 Physician's Desk Reference, addresses the FDA approved uses of ruxolitinib phosphate (Jakafi) to treat myelofibrosis and polycythemia vera. Ex. 1004, 1281. RPI discloses the highlights of prescribing information for Jakafi or ruxolitinib. *Id*. RPI also discloses ruxolitinib formulation information, pharmacodynamic and pharmacokinetic data, clinical trial

results, and dosing recommendations, including the content of ruxulitinib in advised doses. *Id.*, 1282–1287.

4. Alleged Obviousness over Silverman, Xing, and Ruxolitinib Prescribing Information

Petitioner asserts the limitations of claims 1–21 are taught by the combination of Silverman, Xing, and Ruxolitinib Prescribing Information. Pet. 26–32. Petitioner provides a claim chart identifying how Silverman, Xing, and Ruxolitinib Prescribing Information allegedly teach each limitation of claims 1, 8, 9, and 11 and dependent claims 2–7, 10, and 12–21. *Id.*, 69–84. Petitioner's contentions are supported by the declaration testimony of Steven Patterson, Ph.D., (Ex. 1007 ¶¶ 117–246) and Jerry Shapiro, M.D. (Ex. 1009 ¶¶ 15–66).

Patent Owner contends that Ground 1 should be denied because Petitioner has failed to meet its burden to show that the asserted art renders claims 1–21 obvious. Prelim. Resp. 32–43. Patent Owner does not argue any claim individually.

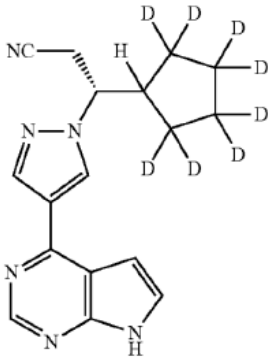
For the reasons discussed below, we determine that Petitioner has demonstrated that it is more likely than not that Petitioner will succeed in showing that the asserted art renders at least one of the challenged claims unpatentable. We provide an analysis of the opposing arguments as they apply to independent claim 1 below, and, following the analysis below, we direct our discussion to the arguments Patent Owner presents in opposition.

a) Independent Claim 1

A method of treating a hair loss disorder in a mammalian subject,

Petitioner argues "Compound (I) [of the '659 patent] is disclosed and claimed in *Silverman* using the designation Compound 111:

Compound 111



Pet. 13. Petitioner contends that Xing discloses the treatment of AA with ruxolitinib and Silverman disclosed that Compound (I) was effective for "treating a disease that is beneficially treated by ruxolitinib." *Id.*, 27 (citing Ex. 1003, 1043, 1048; Ex. 1002, 20:57–59). Therefore, Petitioner argues, the skilled artisan would have found it obvious that Compound (I) could be used for treating a hair loss disorder. *Id.* at 26.

Patent Owner argues Petitioner has not "presented any prior-art disclosures teaching the treatment of AA—or any other hair-loss disorder—with Compound (I) as claimed in the '659 patent." Prelim. Resp. 37. Patent Owner contends Silverman "does *not* disclose the use of ruxolitinib or Compound (I) to treat AA" and the reference to AA in Silverman is directed to the use of a second therapeutic. *Id*. at 37–38 (citing Ex. 1002 at 19:34–50). Patent Owner also argues that none of the reports that Petitioner relies on involved treatment of AA with Compound (I) and the reports do not show treatment of AA at the doses claimed in the '659 patent. *Id.* at 38.

On the current record, Petitioner has made a sufficient showing that the skilled artisan, having read Xing and Silverman, would have found it obvious to use Compound (I) to treat AA based on Silverman's teaching that Compound (I) could be used to treat diseases beneficially treated by ruxolitinib and Xing's success in treating AA with ruxolitinib. The teachings of these references provide both a method of treating, providing Compound (I), and a target hair loss disorder, AA. The artisan would have learned from Xing's prior success in treating AA and have been encouraged by Silverman's explicit guidance to substitute the disclosed compounds for those where ruxolitinib was previously successful, including Silverman's instruction that "guidance for selecting an effective dose can be determined by reference to the prescribing information for ruxolitinib." Ex. 1002, 20:25–27. On this record, we are not persuaded that the artisan would have needed the express teaching Patent Owner suggests given the disclosures discussed above.

> *the method comprising administering to the subject 16 mg/day or 24 mg/day of*

Petitioner contends that the doses required in claim 1 "fall within narrow "effective amounts" ranges of "10 mg to 20 mg" and "5 mg to 25 mg" taught by Silverman for Compound (I)." Pet. 27 (citing Ex. 1002 at 20:9–15). Petitioner also contends, "Silverman further directed that 'guidance for selecting an effective dose can be determined by reference to the prescribing information for ruxolitinib,' (*id*., 20:25–27) which disclosed ranges of 5 to 50 mg per day (EX1004, 4, 5 (*e.g*., §§ 2.4, 2.7) that also narrowly encompass the claimed doses." *Id*.

Patent Owner argues, "the references show anecdotal examples of hair regrowth at doses of ruxolitinib higher than the doses of Compound (I)

claimed in the ’659 patent; in contrast to these prior-art references, the ’659 patent claims lower doses that are supported by a placebo-controlled clinical trial in AA.” Prelim. Resp. 38. Patent Owner also argues Silverman describes doses spanning “from 1 mg to 500 mg” and “fails to teach the specific dose amount of Compound (I) for treatment of AA.” *Id.* at 40 (citing Ex. 1002, 20:10). Specifically, Patent Owner contends that “there is no explanation, other than pure hindsight, to support Incyte’s decision to pluck out these particular examples.” *Id*.

Lastly, Patent Owner argues, “there is nothing about *either* the narrower ranges *or* the broader 1–500 mg range that suggests the two specifically claimed doses of Compound (I) in the ’659 patent, for three independent reasons.” *Id*. at 41. Petitioner argues Silverman does not teach the two doses claimed in the ’659 patent, Silverman’s disclosure of broad ranges of possible doses is not specific to Compound (I), and “none of Silverman’s expansive dose ranges is specific to, or even applicable to, the treatment of AA.” *Id*. at 41−42.

On the current record, Petitioner has made a sufficient showing that the skilled artisan, having read Silverman and RPI, would have found it obvious to administer doses of 16 mg/day or 24 mg/day based on Silverman’s teaching of effective amount ranges of “10 mg to 20 mg” and “5 mg to 25 mg” and based on the prescribing information taught for ruxolitinib in RPI, which Silverman directs the skilled artisan to consult for dosing information, and that also encompasses the claimed doses. Ex. 1004, 4, 5. The artisan would have been encouraged by these relatively narrow ranges and dosing information to follow this guidance, which encompasses and overlaps with the two dosages recited in claim 1. *See, e.g., E.I. DuPont de*

Nemours & Co. v. Synvina C.V., 904 F.3d 996, 1006 (Fed. Cir. 2018) (explaining that where the prior art discloses a range that overlaps with the claimed range there is a "presumption of obviousness"); *In re Applied Materials, Inc.*, 692 F.3d 1289, 1295 (Fed. Cir. 2012) (where the general conditions of a claim are disclosed in the art, "it is not inventive to discover the optimum or workable ranges by routine experimentation" (citing *In re Aller*, 20 F.2d 454, 456 (C.C.P.A. 1955)). In addition, we find persuasive in this regard by the testimony Dr. Patterson that selecting doses within the ranges disclosed by Silverman "would have been a matter of routine optimization" (Ex. 1007 ¶ 173) and that "the POSA would have been additionally motivated to lower doses of Compound (I) compared to ruxolitinib based on the expectation that deuteration would have improved the metabolic stability of ruxolitinib and thus reduced the effective dose relative to ruxolitinib (*id.* at ¶ 198). On this record, we are not persuaded by Patent Owner's argument regarding hindsight.

> *a compound represented by the following structural formula [Compound (I)] or a pharmaceutically acceptable salt thereof*

Petitioner contends Compound (I) and its pharmaceutically acceptable salt are disclosed and claimed in Silverman using the designation Compound 111. Pet. 12–13. Petitioner argues that, during prosecution, the Uttamsingh Declaration was submitted to show the comparative metabolic stability of Compound 111 and two other deuterated ruxolitinib analogs to overcome an obviousness rejection, and that the skilled artisan would have been motivated to use Compound 111 because the data showed Compound 111 was superior to the other two. *Id.* at 15, 34 (citing Ex. 1045 at 377, 416).

Patent Owner contends Petitioner "provides no rationale for why Silverman would have pointed a skilled artisan to Compound 111 specifically" and "Silverman actually discloses [] a genus of compounds of Formula I, and salts thereof." Prelim. Resp. 33. Patent Owner also contends, "person of ordinary skill in the art would affirmatively not have selected Silverman's Compound 111 for further study" because Silverman provides data showing an extension of half-life over ruxolitinib for three compounds other than Compound 111 *Id*. at 35.

On the record before us, Petitioner has made a sufficient showing that that the skilled artisan would have been persuaded by the data disclosed in the Uttamsingh Declaration that Compound 111 was metabolically superior and, for this reason, would have been motivated to use it from among the embodiments taught by Silverman.[8]

> *wherein each position in Compound (I) designated specifically as deuterium has at least 95% incorporation of deuterium.*

Petitioner contends that, "*Silverman* taught the use of Compound (I) having "an isotopic enrichment factor for each designated deuterium atom of… at least 6333.3 (95% deuterium incorporation), at least 6466.7 (97% deuterium incorporation)." Pet. 27–28. (citing Ex. 1002, 4:7−17) (alteration in original). Patent Owner does not specifically respond to Petitioner's argument and evidence. *See generally* Prelim. Resp. Having reviewed Petitioner's contention and supporting evidence, we determine that the

[8] We acknowledge Patent Owner's argument (e.g., Prelim. Resp. 35–36) that the Uttamsingh Declaration is not prior art. As discussed In section III(B) above, we reserve determination of this issue for trial and thus rely on the content of the Uttamsingh Declaration for what it would have disclosed to the skilled artisan for purposes of this Decision.

Petition provides the requisite showing, at this stage of the proceeding, that Silverman teaches or suggests this limitation.

b) Independent Claims 9 and 11

Claims 9 and 11 are identical to Claim 1 except they require "administering to the subject twice a day 8 mg" and "administering to the subject twice per day 12 mg of Compound (I)." Ex. 1001, 25:23–46, 26:1–23. Petitioner contends "[t]hese doses are encompassed by the narrow ranges disclosed by *Silverman* for Compound (I) (EX1002, 20:9–15) and the *Ruxolitinib Prescribing Information* for ruxolitinib (EX1004, 4−5)." Pet. 28. Petitioner also contends, "all three Ground 1 references disclosed twice-daily administration, including *Silverman* for Compound (I) (EX1002, 20:17−18), *Ruxolitinib Prescribing Information* for ruxolitinib (EX1004, 4−5), and *Xing* for ruxolitinib to treat AA (EX1003, 10)." *Id*. Having reviewed Petitioner's contention and supporting evidence, we determine that the Petition provides the requisite showing, at this stage of the proceeding, that Silverman teaches or suggests this limitation.

c) Dependent claims 2–7, 10, and 12–21

Claims 2, 15, and 18 recite that "the hair loss disorder is alopecia areata." Petitioner contends "Silverman disclosed that Compound (I) can be used for diseases treated by ruxolitinib and Xing disclosed treatment of AA with ruxolitinib." *Id*. at 29.

Claims 3, 16, and 19 require oral administration. Petitioner contends "[c]laims 3, 16, and 19 was disclosed by all three Ground 1 references, including for Compound (I) (EX1002, 17:18−21), for ruxolitinib (EX1004, 4, 6 (*e.g.*, § 2.9), 7 (*e.g.*, § 11)) and ruxolitinib for the treatment of AA (EX1003, 10)." *Id*. at 30. Petitioner also contends administration as a tablet

and administration to a human were disclosed by each of the references Silverman, Xing, and Ruxolitinib Prescribing Information. *Id*.

Claim 5 requires once daily administration. Petitioner contends "Silverman disclosed the effective amount of Compound (I) administered once a day" and Ruxolitinib Prescribing Information disclosed patients maintain a does at 5 mg once daily if on 5 mg once daily of ruxolitinib. *Id*.

Claim 7 recites "Any atom not designated as deuterium is present at its natural isotopic abundance." Petitioner contends, "[t]]his limitation is disclosed verbatim by *Silverman* for Compound (I)." *Id*. (citing Ex. 1002, 9:28−30, 12:20−21). Petitioner also contends "97% deuterium incorporation is expressly disclosed by *Silverman* for Compound (I)." *Id*. 30−31 (citing Ex. 1002, 4:7−17).

Claims 10 and 12 require administration of Compound (I) as a phosphate salt. Petitioner contends, "*Silverman* taught Compound (I) as a pharmaceutically acceptable salt and expressly disclosed "[s]uch pharmaceutically acceptable salts thus include… phosphate…." *Id*. at 31 (citing Ex. 1002, 5:6–24). Petitioner also contends "*Ruxolitinib Prescribing Information* disclosed "Each tablet contains ruxolitinib phosphate" (EX1004, 7) and *Xing* disclosed treating AA with "FDA-approved" ruxolitinib, (EX1003, 10), which is ruxolitinib phosphate (EX1004, 7 (*e.g.*, § 11)." *Id*.

Patent Owner does not specifically respond to Petitioner's arguments and evidence on any dependent claim. *See generally* PO Resp. Having reviewed Petitioner's contentions and supporting evidence, we determine that the Petition provides the requisite showing, at this stage of the

proceeding, that Silverman, Xing, and RPI teach or suggest each limitation of the dependent claims as alleged by Petitioner.

5. Motivation to Combine Silverman, Xing, and Ruxolitinib Prescribing Information

Petitioner argues "A POSA would have been motivated to orally administer tablets of Compound (I) according to *Silverman* to treat AA, which *Xing* taught could be treated in humans with orally administered tablets of ruxolitinib, (1) based on the express teaching of *Silverman*, (2) based on the expectation of obtaining at least the same efficacy as ruxolitinib, and/or (3) to obtain improved pharmacokinetic properties via deuteration." *Id.* at. 33 (citing Ex. 1007, ¶¶ 38−43, 126−135). Petitioner points to Silverman's disclosure of Compound (I) as useful in treating diseases and conditions beneficially treated by ruxolitinib. *Id*. at 34. Petitioner also states, "given that Xing taught that AA was 'beneficially treated by ruxolitinib' (EX 1002, 20:57−61), a POSA would have been motivated to use its deuterated analog—particularly Compound (I) — to achieve at least equally efficacious treatment of AA". *Id*. at 34–35 (citing Ex. 1007, ¶¶ 122−126).

Patent Owner presents three main arguments that Petitioner fails to meet its burden to show there was a motivation for a person of ordinary skill in the art to substitute Compound (I) for ruxolitinib. Prelim. Resp. 43−50. First, Patent Owner argues that "Silverman is not a proper prior-art reference, and even if it were, it contains no data for Compound (I) (or "Compound 111") that would have motivated a person of ordinary skill in the art to select that compound from among the compounds disclosed." *Id*. at 43−44. Second, Patent Owner argues that Petitioner has no evidence "that there was a known relationship between the pharmacokinetic and

pharmacodynamic properties of ruxolitinib, which would have allowed a skilled artisan to predict therapeutically effective doses for the treatment of AA." *Id*. at 44−45. Specifically, Patent Owner contends that Petitioner "has certainly not shown a known pharmacokinetic/pharmacodynamic relationship for Compound (I)." *Id*. Third, Patent Owner argues that Petitioner "has failed to cite any prior art suggesting effective treatment of AA with ruxolitinib at a dose lower than 30 mg/day, and certainly not at the claimed doses of 16 mg/day or 24 mg/day." *Id*. at 46.

a) Motivation to Substitute Compound (I) for Ruxolitinib

Petitioner presents expert testimony supporting its argument that a skilled artisan would have been motivated by a continuing need to discover drugs to treat conditions for which ruxolitinib was used, which would have included AA, for which ruxolitinib had demonstrated clinical efficacy. Ex. 1007 ¶¶ 126–128 (citing Christiano and Xing as examples). Dr. Patterson opines that a skilled artisan would have been motivated to substitute Compound (I) for ruxolitinib to arrive at the claimed subject matter, including because deuterium substitution of a drug was demonstrated to reduce the overall drug dose required and to increase bioavailability of the drug with a minimal impact on the effectiveness. Pet. 15, 33–57; Ex. 1007 ¶¶ 129–133; see also Ex. 1001, 2:7–8 ('659 patent statement indicating deuterium modification is a "potentially attractive strategy for improving a drug's metabolic properties.").

As discussed above, Petitioner has shown sufficiently for institution that a person of ordinary skill in the art, having read Silverman and the Uttamsingh Declaration submitted to show the comparative metabolic stability of Compound 111 and two other deuterated ruxolitinib analogs to

overcome an obviousness rejection, would have been motivated to select Compound 111/Compound (I) based on its demonstrated superior metabolic data and pursue it in treating conditions including AA as opposed to ruxolitinib. Ex. 1045, 390–407, 414–417. We are not persuaded by Patent Owner's argument that references such as Xing that show experimental examples of hair growth at high doses of ruxolitinib would not have motivated the skilled artisan to pursue treatment of AA with Compound (I); rather, on the current record, we find these references would have strongly motivated the skilled artisan to pursue such treatment, particularly with the deuterated compound expected to provide greater bioavailability at lower doses. Ex. 1007 ¶¶ 129–133.

b) Motivation to Optimize Dosing Regimen

Petitioner argues that

> [a] POSA would have been motivated with a reasonable expectation of success to use Compound (I) in the treatment of AA with the claimed dosing regimen, *i.e.*, orally administered (Claims 3, 16, 19) tablets (Claim 4) of 16 mg/day or 24 mg/day (Claims 1−7, 9−21) QD (Claim 5), 8 mg BID (Claims 6, 9−10), and 12 mg BID (Claims 11−12).

Pet. 43. Petitioner contends,

> [t]he claimed 16 and 24 mg/day doses (1) fall within the narrow range disclosed by *Silverman* and *Ruxolitinib Prescribing Information*; (2) were suggested based on the strong clinical response seen at 30 and 40 mg per day of ruxolitinib; (3) fall within a narrow range suggested by the dose-response relationships for ruxolitinib and closely-related baricitinib; and (4) were suggested by the potential for reduced dosing due to deuterium-inhibited metabolism.

Id. Petitioner also contends a person of ordinary skill in the art would have been motivated to administer the claimed doses QD (once per day) and BID

(twice per day). *Id*. at 51. Lastly, Petitioner contends "[a] POSA would have been motivated to administer Compound (I) as a phosphate salt at doses of 10.5 mg and 15.8 mg (Claims 10, 12), which correspond to 8 mg and 12 mg of Compound (I) free base together with the additional phosphate salt mass." *Id*. at 53−54.

Patent Owner argues that Petitioner failed to meet its burden to show that there was a motivation to select the claimed doses and regimen. Prelim. Resp. 50−66. First, Patent Owner argues Petitioner improperly relies on related drugs in sister diseases to assert a motivation to use the claimed doses of Compound (I) of AA. *Id*. at 51−57. Patent Owner challenges Petitioner's reliance on dosing for other JAK inhibitor drugs (e.g., ruxolitinib, tofacitinib, and baricitinib) as support for its position that a person of skill in the art would have been motivated to use the claimed doses of Compound (I). *Id*. at 54. Patent Owner also contends that Petitioner's reliance on baricitinib dosing to predict ruxolitinib or compound (I) dosing ignores the different metabolism of the two drugs. *Id*. at 55. Patent Owner contends that Petitioner attempts to rely on irrelevant mathematical calculations to determine ruxolitinib dosing from barcitinib dosing. *Id*. at 56.

While we agree with Patent Owner that the positive effects of related drugs on sister diseases may not be strong evidence supporting the potential positive effect of Compound (I), it is evidence that, considered with other evidence in totality and absent any evidence to the contrary, does contribute to the overall motivation the skilled artisan would have had to pursue treating AA with Compound (I). On the current record, we find persuasive Dr. Patterson's testimony that the success of these drugs in sister diseases

was achieved by regulation of the same JAK/STAT pathway that ruxolitinib is effective in treating as well as Christiano's "extensive preclinical data demonstrating the efficacy of JAK inhibitors to treat AA including results from *in vitro* assays and administration of JAK inhibitors to mouse models of AA." Ex. 1007 ¶¶ 60–61.

We acknowledge Patent Owner's additional arguments that Petitioner improperly relies on art published after the '659 patent's priority date on ruxolitinib for motivation to use lower doses (Prelim. Resp. 58−59) prior-art dosing disclosures on which Petitioner relies on would not have lead a person of ordinary skill in the art to the claimed doses (*id.* at 59−60), and that Petitioner "cannot rely on a skilled artisan's general "prefer[ence] to use the lowest dose and dosing frequency sufficient to achieve effective therapy" because it does not supply the motivation to use the specific doses claimed from Compound (I) for the treatment of AA (*id.* at 66) (alteration in original). Each of these may have some individual merit, but we find, on balance and on the current record, that Patent Owner's arguments in the Preliminary Response are outweighed by the showing in the Petition.

Petitioner has shown sufficiently for institution that an artisan would have been motivated to combine the teachings of Silverman, Xing, and Ruxolitinib Prescribing Information. Based on the record before us, for the purposes of institution, we find Petitioner has made a sufficient showing that the teachings of these references provided a motivation to substitute Compound (I) for ruxolitinib and a motivation to use Compound (I) in treatment of AA with the claimed dosing regimen. In addition, we find Petitioner has made a sufficient showing that the artisan would have been motivated to combine the teachings from Silverman and RPI guidance on

administration of oral doses. Ex. 1002, 20:9–15; Ex. 1004, 4–6. Similarly, for the purposes of institution, the artisan would also have been motivated to combine the teachings of Silverman, RPI, and Xing to treat AA using once or twice daily dosing. Ex. 1002, 15−18; Ex. 1003, 10; Ex. 1004, 4–6. Lastly, we find Petitioner has made a sufficient showing that the artisan would have been motivated to administer Compound (I) as a phosphate salt based on Silverman's disclosure. Ex. 1002, 4:62–5:8.

H. Ground 2

1. Silverman (Ex. 1002)

Petitioner relies on the same teachings from Silverman for its allegations of obviousness in Ground 2 as were applied to Ground 1 above. Pet. 62, 69–84.

2. Christiano (Ex. 1005)

Christiano discloses "methods for treating a hair loss disorder in a subject by administering a Janus Kinase/Signal Transducers and Activators of Transcription inhibitor." Ex. 1005, Abstract. According to Christiano, the inhibitor is a JAK1, JAK2, and/or a JAK3 inhibitor, a Stat1 and/or a Stat2 inhibitor, INCB018424 (ruxolitinib) or tofacitinib (CP690550). *Id*. at 1:67−2:4. Christiano discloses that alopecia areata is among the hair loss disorders targeted for treatment in the method. *Id*. at 2:4−6. Christiano also states, "the method further comprises determining whether the inhibitor administered induced hair growth in the subject afflicted with a hair loss disorder as compared to the subject's hair growth prior to treatment with the inhibitor." *Id*. at 2:9−12. Christiano discloses the treatment of mice with JAK3 inhibitors prevents alopecia areata. Ex. 1005, 6:36−37. Christiano reports treatment of dermal T cell infiltrates and inflammatory biomarkers

by immunostaining and by flow cytometry. Id. at 1005, 6:38−40 (citing Figure 33A; 33B). The results showed an association between CD8+ T-cells, proinflammatory cytokines (IFN-γ), the JAK-STAT pathway in AA patients, and other data supporting the use of JAK inhibitors to treat AA. Id. at 4:21−12:39.

3. Ni (Ex. 1006)

Ni discloses "sustained-release formulations and dosage forms of ruxolitinib, or a pharmaceutically acceptable salt thereof, which are useful in the treatment of Janus kinase-associated diseases such as myeloproliferative disorders." Ex. 1006 ¶ 1. "Ruxolitinib . . . is the first FDA approved Janus kinase (JAK) inhibitor and is the only drug currently approved for treatment of myelofibrosis." *Id.* ¶ 2. "To date, all published human clinical data for ruxolitinib relate to dosing of an immediate-release formulation." *Id.* ¶ 3. The "[i]mmediate-release dosage forms of ruxolitinib phosphate can be obtained commercially in 5, 10, 15, 20, and 25 mg doses as the drug product Jakafi® (ruxolitinib phosphate (tablets)) (NDA no. N202192)." *Id.* ¶ 124. Ni also discloses a bioavailability study "exploring the safety, tolerability, and efficacy of ruxolitinib, administered orally to patients with primary myelofibrosis (PMF) and post poly cythemia vera/essential thrombocythemia myelofibrosis (Post-PV/ET MF)." *Id.* ¶ 137. The study evaluated "two dose levels of 25 mg bid and 50 mg bid," "five dose regimens of 10 mg bid, 25 mg bid, 25 mg qd, 50 mg qd and 100 mg qd," and "six dose regimens of 10 mg bid, 15 mg bid, 25 mg bid, 50 mg qd, 100 mg qd and 200 mg qd." *Id.*

4. Alleged Obviousness over Silverman, Christiano, and Ni

Petitioner contends "all limitations of claims 1–21 are also taught by *Silverman* in view of *Christiano* (EX1005) and *Ni* (EX1006)." Pet. 62, 69–84. Petitioner's contentions are supported by testimony from Dr. Patterson. *Id*. (citing Ex. 1007 ¶¶ 247–281). Petitioner contends "a POSA would have been motivated to select Compound (I) from *Silverman* to "treat[] a disease that is beneficially treated by ruxolitinib in a subject in need thereof," such as AA, as it was (1) deuterated at ruxolitinib's "metabolic hotspots," (2) amongst the compounds showing the greatest potential for improvement in metabolic stability, and (3) one of three compounds specifically claimed by *Silverman*." *Id*. at 62. (citing Ex. 1002, 20:51−62; Ex. 1007 at ¶ 251) (alteration in original). Petitioner also contends that the skilled artisan "would have been motivated to combine *Silverman*'s Compound (I)—a JAK inhibitor—with *Christiano* to treat AA in view of *Christiano's* disclosure of using ruxolitinib specifically and JAK inhibitors generally to treat AA." *Id*. at 63 (citing Ex. 1005 at 2:1−9, 4:21−12:39, 113:1−6, 271:30−39; Ex. 1007 at ¶¶ 248−250) (footnote omitted). Lastly, Petitioner contends the skilled artisan would have been "further motivated to combine the references by *Silverman*'s disclosure that Compound (I) was useful for diseases 'beneficially treated by administering an inhibitor of Janus-associated kinase with selectivity for subtypes 1 and 2 (JAK1/JAK2)… [and] beneficially treated by ruxolitinib.'" *Id*. (citing Ex. 1002, 3:27−32, 20:57−61) (alteration in original).

At this stage of the proceeding, Patent Owner does not raise any arguments with respect to Petitioner's contentions directed to Christiano and Ni. *See generally* Prelim. Resp. On the record before us, we find that

Petitioner has demonstrated that it is more likely than not that the skilled artisan would have been motivated to combine the teachings of Silverman, Christiano, and Ni to make the claimed subject matter.

With respect to the claimed dosing regimen, Petitioner contends that the skilled artisan would have been motivated to treat AA using orally administered tablets of Compound (I) as claimed at least because these elements were "taught to be effective for ruxolitinib, and 'formulations issues' and 'delivery options' would not have been expected to be affected by the deuterium substitution in Compound (I)." Pet. 63−64 (citing Ex. 1033, 8−9; Ex. 1007 at ¶¶ 49, 260−263). Petitioner argues "*Ni* disclosed oral administration of tableted ruxolitinib to humans" and Christiano disclosed the use of ruxolitinib to treat AA. *Id*. at 64 (citing, e.g., Ex. 1006 ¶ 12; Ex. 1005, 78:36–38).

Petitioner contends that in light of the teachings of the references, the skilled artisan "would have been motivated and had a reasonable expectation of success to administer the claimed daily doses using QD and BID dosing frequencies." *Id.* at 65 (citing Ex. 1007, at ¶¶ 257−258; Ex. 1009 ¶¶ 44−47). Petitioner argues that "*Christiano* taught QD and BID dosing for JAK inhibitors, which would have included and provided motivation for QD and BID dosing of Compound (I), a JAK inhibitor" and "*Silverman* and *Ni* also disclosed, and would have motivated, using QD and BID dosing." *Id*. (citing Ex. 1005, 93:40−44; Ex. 1002, 20:15−18; Ex. 1006 ¶¶147, 157; Ex. 1007 ¶¶ 257−258).

Lastly, Petitioner contends that "[a] POSA would have been motivated to administer Compound (I) as a phosphate salt at doses of 10.5 and 15.8 mg BID" and that the skilled artisan "would have reasonably

expected that the use of Compound (I) as claimed would at least 'treat' AA as defined by the '659 Patent." *Id*. 66−67 (citing Ex. 1002, 5:6−24; Ex. 1006 ¶ 124).

At this stage of the proceeding, Patent Owner has not does not raise additional arguments with respect to Petitioner's contentions directed to Christiano and Ni. *See generally* Prelim. Resp. On the record before us, we agree that the skilled artisan would have been motivated to create the orally administered dosing regimen of the challenged claims.

5. Reasonable Expectation of Success

Petitioner contends that the skilled artisan would have had a reasonable expectation of success in making the claimed compositions comprising Compound (I). Pet. 57−61. Petitioner contends, "[o]rally administered tablets of ruxolitinib phosphate were known to effectively treat AA in humans." *Id*. at 57 (citing Ex. 1003, 1048; Ex. 1088, 13 (Higgins article); Ex. 1012, 6 (Pieri article); Ex. 1031, 9 (Harris article); Ex. 1009 ¶¶ 19−28; Ex. 1007 ¶¶ 22−37). Petitioner argues that the skilled artisan "would have expected that orally administered tablets of Compound (I) phosphate—which differs structurally from ruxolitinib only in the replacement of eight hydrogens with deuterium—would likewise have been effective in treating AA in humans." *Id*. citing (Ex. 1007 ¶¶ 235−239; Ex. 1009 ¶¶ 48−51; Ex. 1002, 2:15−20; Ex. 1038, 5). Petitioner also contends that the "expectation would have applied equally where each deuterium in Compound (I) has an isotopic purity of least 97% and all other atoms are present at their natural isotopic abundance." *Id*. at 58 (citing Ex. 1007 ¶¶ 164, 235).

Further, Petitioner argues, "a POSA would have had a reasonable expectation of success for treating AA with Compound (I) at the claimed doses and frequencies, including doses of 16 mg and 24 mg administered QD or BID and phosphate equivalents (10.5 or 15.8 mg) administered BID." *Id*. at 59 (citing Ex. 1007 ¶¶ 240−244; Ex. 1009 ¶¶ 48−51). Petitioner asserts that "there would have been a reasonable expectation of success as the claimed doses fall within narrow ranges of 5 to 25 mg/day for Compound (I) taught by *Silverman* and 5 to 50 mg/day taught by *Ruxolitinib Prescribing Information* for ruxolitinib." *Id*. at 59. Petitioner also contends that "a POSA would have reasonably expected that doses of Compound (I) in the range of ~10 mg/day to 50 mg/day would at least have provided "regrowth of hair, prevention of further, hair loss, or diminishing the rate of hair loss," given that a total daily dose of 30 mg resulted in durable hair regrowth in AA. *Id*. at 60 (citing Ex. 1001, 5:66−6:5, Ex. 1009 ¶¶ 48−51; Ex. 1007 ¶¶ 179−180, 195−197). Petitioner states "there was a reasonable expectation that both QD and BID administration of Compound (I) at the claimed doses would have treated AA for the same reasons a POSA would have been motivated to use these dosing intervals." *Id*. at 61 (citing Ex. 1007 ¶¶ 243−244).

Patent Owner argues that Petitioner has not met its burden to show there is a reasonable expectation of success. Prelim. Resp. 66. Specifically, Patent Owner argues that the use of clinical reports to support the proposition that ruxolitinib was known to effectively treat AA in humans is "insufficient to provide a reasonable expectation of success in treating patients with AA with ruxolitinib, let alone with Compound (I) at the claimed doses." *Id*. at 66−67. Patent Owner states, "[t]aken individually or

together, these references do not support a reasonable expectation of success, particularly at the claimed doses of 16 mg to 24 mg a day given the lowest reported dose of ruxolitinib that was given was 30 mg per day." *Id*. at 68.

On the current record, we are not persuaded by Patent Owner's argument that Petitioner has not met its burden to show there is a reasonable expectation of success. Petitioner offers the testimony of Dr. Patterson to support the assertion that the skilled artisan would have had a reasonable expectation of success in making the claimed compositions for treatment of AA. *See, e.g.*, Ex. 1007 ¶¶ 243−244. At this stage of the proceeding, Patent Owner has not presented contrary evidence from a qualified witness as to what a skilled artisan would have learned from these trials. We find the evidence currently of record demonstrates that it is more likely than not that the skilled artisan would have had reasonable success in treating patients with AA using Compound (I) at the claimed doses. Patent Owner may challenge this evidence at trial.

6. Secondary Considerations

Secondary considerations include, *inter alia*, long-felt but unsolved needs, failure of others, and unexpected results. *In re Rouffet*, 149 F.3d 1350, 1355 (Fed. Cir. 1998). With respect to the last of these, our reviewing court emphasizes that "[u]nexpected results that are probative of nonobviousness are those that are 'different in kind and not merely in degree from the results of the prior art.'" *Galderma Labs., LP v. Tolmar, In*c., 737 F.3d 731, 739 (Fed Cir. 2013) (quoting *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004). Results which differ by percentages are differences in degree rather than kind, where the

modification of the percentage is within the capabilities of one skilled in the art at the time. *See In re Harris*, 409 F.3d 1339, 1344 (Fed. Cir. 2005) ("32–43% increase in stress-rupture life . . . does not represent a 'difference in kind' that is required to show unexpected results").

"For objective evidence of secondary considerations to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *ClassCo, Inc. v. Apple, Inc*., 838 F.3d 1214, 1220 (Fed. Cir. 2016) (citing *In re Kao*, 639 F.3d 1052, 1068 (Fed. Cir. 2011)). The question of nexus is highly fact specific and it is Patent Owner's burden to establish a sufficient nexus. *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019). A patentee is entitled to a rebuttable 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.'" *Id.*

Petitioner argues that "[n]o unexpected results or other secondary indicia of nonobviousness were relied upon during prosecution of the '659 Patent" and reserves the right to rebut any such evidence. Pet. 84. Petitioner discusses Phase II trial results for Compound (I), which Patent Owner had relied on during patent prosecution (Ex. 1089, 4), and asserts the studies show no unexpected superiority. *Id.* 84–85.

Patent Owner argues that secondary considerations support a finding of nonobviousness and the information presented by Petitioner does not repudiate that evidence. Prelim. Resp. 68–69. Specifically, Patent Owner argues that the Phase II evidence cited by Petitioner "supports the unexpected efficacy of Compound (I) in treating AA." *Id*. at 69. Patent Owner contends "[t]here is no prior art that provides an effective treatment

for AA at the claimed doses using ruxolitinib, let alone Compound (I)." *Id*. Patent Owner cites as evidence its own press release describing "Positive CTP-543 Results from Phase 2 Alopecia Areata Trial." Ex. 2026. Patent Owner's contentions, however, are presently unsupported by expert testimony and may benefit from further development and testing at trial.

We have reviewed Patent Owner's cited evidence and have considered it along with Petitioner's evidence of obviousness. In weighing the totality of the evidence of record and the strength of the parties' showings on the inquiries underlying the question of obviousness, we conclude that Petitioner has met its overall burden of proving that it is more likely than not that at least one of the claims challenged in the petition is unpatentable.

IV. CONCLUSION

For the foregoing reasons, we conclude that the information presented in the Petition demonstrates that it is more likely than not that claims 1–7 and 9–21 are unpatentable.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 324(a), a post-grant review of claims 1–7 and 9–21 of U.S. Patent No. 10,561,659 B2 is instituted with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that notice is hereby given of the institution of a trial which will commence on the entry date of this Decision.

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