Trials@uspto.gov
571.272.7822

Paper No. 9
Entered: October 19, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INCYTE CORPORATION,
Petitioner,

v.

CONCERT PHARMACEUTICALS, INC.,
Patent Owner.

Case IPR2017-01256
Patent 9,249,149 B2

Before MICHAEL J. FITZPATRICK, ZHENYU YANG, and TINA E. HULSE, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

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

I. INTRODUCTION

Incyte Corporation ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–15 of U.S. Patent No. 9,249,149 B2 (Ex. 1001, "the '149 patent"). Paper 1 ("Pet."). Concert Pharmaceuticals, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp.").

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a); *see also* 37 C.F.R. § 42.4(a) (stating Director has delegated institution authority to Board). Upon considering the Petition and Preliminary Response, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–15 of the '149 patent. Accordingly, we decline to institute an *inter partes* review of those claims.

A. Related Proceedings

The parties identify pending U.S. Patent Application No. 14/570,954 as a related matter to this proceeding. Pet. 1; Paper 5, 1. The '149 patent is a continuation of that application.

B. The '149 Patent

The '149 patent is entitled "Deuterated Derivatives of Ruxolitinib," and issued on February 2, 2016. Ex. 1001, [54], [45]. According to the '149 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 1:28–31. Another ADME limitation is the formation of toxic or biologically reactive metabolites. *Id.* at 1:39–40.

The cytochrome P450 enzyme ("CYP") is typically responsible for hepatic metabolism of drugs. *Id.* at 1:52–54. As such, the '149 patent identifies deuterium modification as a "potentially attractive strategy for improving a drug's metabolic properties." *Id.* at 2:5–6. 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 2:6–10. 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.

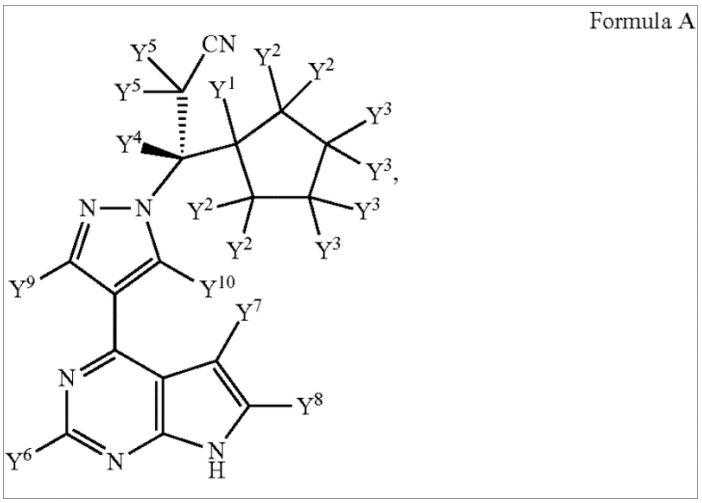
According to the '149 patent, however, studies measuring deuterium substitution's effect on overall metabolic stability have reported variable and unpredictable results. *Id.* at 2:32–35. The '149 patent explains that the effects of deuterium modification on a drug's metabolic properties are not predictable "even when deuterium atoms are incorporated at known sites of metabolism." *Id.* at 2:42–44. As such, the specification states that determining whether and how deuterium modification affects the metabolism rate of a drug requires actually preparing and testing the deuterated drug. *Id.* at 2:44–47. Thus, the '149 patent states that "[t]he site(s) where deuterium substitution is required and the extent of deuteration necessary to see an effect on metabolism, if any, will be different for each drug." *Id.* at 2:49–52.

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 2:53–67. Ruxolitinib also has other potential applications, including the treatment of essential thrombocytopenia, psoriasis, and various forms of cancer. *Id.* at 3:3–6. 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 3:19–21.

C. Illustrative Claim

Petitioner challenges claims 1–15 of the '149 patent, of which claims 1 and 9 are the only independent claims. Claim 1 is illustrative and is reproduced below:

1. A compound of Formula A:



or a pharmaceutically acceptable salt thereof, wherein:

Y^1 is a hydrogen;

each Y^2 is selected from hydrogen and deuterium, and each Y^2 is the same;

each Y^3 is selected from hydrogen and deuterium, and each Y^3 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:

each Y^2 is deuterium; or

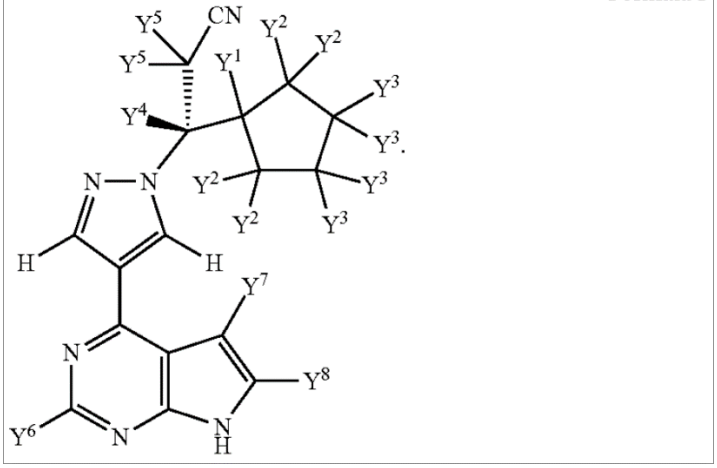
each Y^3 is deuterium; or

each Y^2 and each Y^3 is deuterium.

Ex. 1001, 36:17–53.

Claim 9 is similar to claim 1, but is directed to Formula I, which is reproduced below:

Formula I



Formula I is similar to Formula A, but Y^9 and Y^{10} of Formula A are both hydrogen in Formula I.

Claims 2–7 and 10–14 depend from claim 1 or claim 9 and recite specific deuteration patterns of ruxolitinib. Claims 8 and 15 depend from claim 1 and claim 9, respectively, and recite a

pharmaceutical composition of claim 1 or claim 9, and a pharmaceutically acceptable carrier.

D. Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–15 of the '149 patent on the following grounds:

Reference(s)	**Basis**	**Claims challenged**
Jakafi Label,[1] Shilling,[2] and Concert Backgrounder[3]	§ 103	1–15
Rodgers[4]	§ 102	1–15
Rodgers, Shilling, and Concert Backgrounder	§ 103	1–15

Petitioner also relies on the Declaration of F. Peter Guengerich, Ph.D. (Ex. 1002).

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art as of June 15, 2012, would have had a "master's degree or a Ph.D. in chemistry, biochemistry, pharmaceutics, pharmaceutical sciences, physical organic chemistry or a related discipline," or a lesser degree with more experience.

---

[1] Jakafi Prescribing Information (revised 11/2011). ("Jakafi Label," Ex. 1004),
[2] Shilling et al., *Metabolism, Excretion, and Pharmacokinetics of [^{14}C]INCB018424, a Selective Janus Tyrosine Kinase ½ Inhibitor, in Humans*, 38 DRUG METABOLISM AND DISPOSITION 2023–31 (2010) ("Shilling," Ex. 1005).
[3] CoNCERT Pharmaceuticals, Inc. Precision Deuterium Chemistry Backgrounder ("Concert Backgrounder," Ex. 1006).
[4] Rodgers et al., US 7,598,257 B2, issued Oct. 6, 2009 ("Rodgers," Ex. 1007).

Pet. 9 (citing Ex. 1002 ¶¶ 15–18). Patent Owner does not contest Petitioner's description of the level of ordinary skill in the art in its Preliminary Response. Prelim. Resp. 27.

On this record, we adopt Petitioner's uncontested description of the level of ordinary skill in the art. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

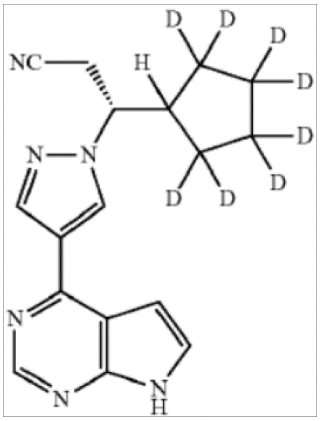
B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, and absent any special definitions, we generally give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

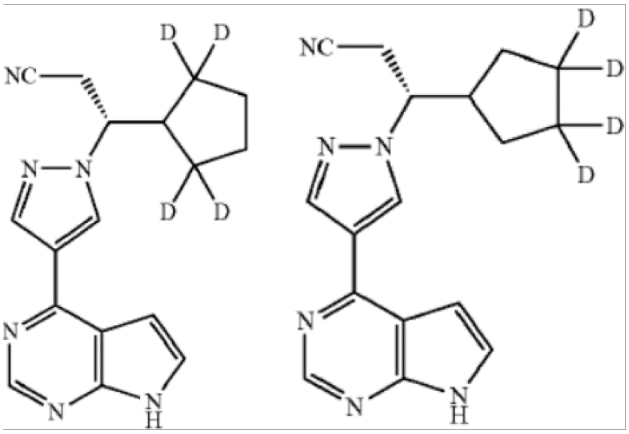
We determine that it is unnecessary to expressly construe any claim terms for purposes of this Decision. *See Wellman, Inc. v. Eastman Chem.*

Co., 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

We note, however, that Petitioner limits its analysis to three compounds that it contends are covered by each of the claims. Specifically, Petitioner asserts that claims 1, 2, 5–7, 9, 10, 13, and 14 each read on the following "octa-deuterated" ruxolitinib analog, which is reproduced below:



Pet. 8. The "octa-deuterated" ruxolitinib analog replaces each Y^2 and Y^3 hydrogen with deuterium. Petitioner also asserts that claims 1–4, 6, 7, 9–12, and 14 each read on the following "tetra-deuterated" ruxolitinib analogs, which are reproduced below:



Id. The "tetra-deuterated" ruxolitinib analogs replace each Y^2 or each Y^3 hydrogen with deuterium. Patent Owner does not dispute Petitioner's contention.

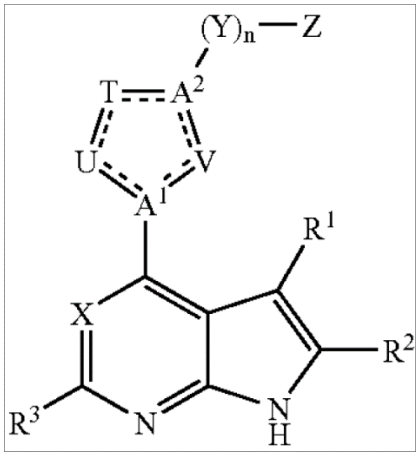
Having considered the compounds and the claims, we agree with Petitioner that the cited claims encompass the three compounds.

C. Anticipation by Rodgers

Petitioner asserts claims 1–15 are anticipated by Rodgers. Pet. 43–50. Patent Owner opposes Petitioner's assertion. Prelim. Resp. 59–70. On this record, we determine Petitioner has not shown a reasonable likelihood of prevailing on its assertion.

1. Rodgers (Ex. 1007)

Rodgers relates to heteroaryl substituted pyrrolo[2,3-b]pyridines and heteroaryl substituted pyrrolo[2,3-b]pyrimidines that modulate the activity of Janus kinases and are useful in treating diseases related to the activity of Janus kinases. Ex. 1007, 1:18–22. The compounds of Rodgers's invention have "Formula I," including pharmaceutically acceptable salt forms or prodrugs. An illustration of Rodgers's Formula I is reproduced below:



Id. at 7:20–37. Rodgers's Formula I, reproduced above, includes numerous possibilities for each constituent member. *Id.* at 7:38–11:20. Rodgers states

that its invention includes all stereoisomers, such as enantiomers and diastereomers (unless otherwise indicated). *Id.* at 31:32–34. Compounds of the invention also include "all isotopes of atoms occurring in the intermediates or final compounds. . . . For example, isotopes of hydrogen include tritium and deuterium." *Id.* at 32:13–17. Claims 1–3 recite ruxolitinib and its isomer. *Id.* at 374:12–20 (claims 1–3).

2. Analysis

Anticipation requires that "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). Anticipation may arise where a reference describes a "definite and limited class," and a person of ordinary skill in the art would "at once envisage each member of this limited class." *In re Petering*, 301 F.2d 676, 681 (CCPA 1962).

According to Petitioner, Rodgers claims ruxolitinib and further explains in the specification that "deuterated forms of the claimed ruxolitinib compounds are within the scope of the invention." Pet. 44 (citing Ex. 1007, 32:13–17). Thus, Petitioner contends that, reading Rodgers as a whole, a person of ordinary skill in the art "would immediately envisage from Rodgers a genus of deuterated ruxolitinib analogs." *Id.* at 45 (citing Ex. 1002 ¶¶ 131–132).

Specifically, Petitioner asserts that although there are 18 hydrogens in ruxolitinib, a person of ordinary skill in the art would immediately realize that there are only ten possible distinct sites of deuteration on ruxolitinib. *Id.* at 45–46 (citing Ex. 1002 ¶ 131). Those ten possible sites are consistent with those identified by Formula A of the '149 patent. *Id.* at 46–47 (citing

Ex. 1001, 6:7–50). From this, Petitioner and its declarant assert that the potential number of deuterated analogs is 2^{10}-1, or 1,023. *Id.* at 47; Ex. 1002 ¶ 131. And, although 1,023 is a large number, Petitioner argues that a person of ordinary skill in the art would be able to at once envisage each compound, because each option "is merely a binary choice of 'H' or 'D.'" Pet. 47; Ex. 1002 ¶ 131.

We are not persuaded by Petitioner's argument. We agree rather with Patent Owner that Rodgers's disclosure is not as focused as Petitioner contends. Prelim. Resp. 59–62. Even assuming a person of ordinary skill in the art would choose to start with ruxolitinib from the potentially trillions of compounds taught by Rodgers, we do not find Rodgers's disclosure of deuterium to be a "binary choice," as characterized by Petitioner. Pet. 47. Rather, Rodgers broadly states that compounds of the invention can also include "*all* isotopes of atoms occurring in the intermediates or final compounds. . . . For example, isotopes of hydrogen include tritium and deuterium." Ex. 1007, 32:13–17 (emphasis added). Thus, Rodgers teaches that deuterium (along with tritium) is just an example of an isotope of hydrogen. *Id.* Rodgers, however, does not focus on that specific example, let alone on the deuterium option or the tritium option within that example. Instead, it generally discloses the substitution of any isotope of any atom in any intermediate or final compound. *Id.* Thus, Petitioner has not shown sufficiently that Rodgers identifies deuterium as a preferred isotope that would narrow the genus of ruxolitinib analogs. *See Ineos USA LLC v. Berry Plastics Corp.*, 783 F.3d 865, 872 (Fed. Cir. 2015) (finding anticipation based on disclosure of a "narrower preferred genus" of saturated fatty acid amides having 12–35 carbons); *In re Schaumann*, 572 F.2d 312, 314–15

(CCPA 1978) (finding anticipation where explicit "pattern of preferences" for lower alkyl secondary amines narrowed the genus to seven possible compounds).

Accordingly, we are not persuaded that Rodgers identifies a "definite and limited class" of deuterated ruxolitinib analogs that would allow a person of ordinary skill in the art to "at once envisage *each* member of this *limited* class." *Petering*, 301 F.2d at 681 (emphasis added). Rather, in light of the lack of preferences for isotopes encompassed by the invention, we find Rodgers to be a "broad generic disclosure" of a "vast" number of compounds. *See id.*

Having considered the arguments and evidence, we determine Petitioner has not shown a reasonable likelihood of prevailing on its assertion that any of the challenged claims are anticipated by Rodgers.

D. Obviousness Grounds

In Ground 1, Petitioner asserts that claims 1–15 of the '149 patent are unpatentable as obvious over the combination of Jakafi Label, Shilling, and Concert Backgrounder. Pet. 26–43. In Ground 3, Petitioner asserts that claims 1–15 are unpatentable as obvious over the combination of Rodgers, Shilling, and Concert Backgrounder. Pet. 50–55. Patent Owner opposes Petitioner's assertions. Prelim. Resp. 27–59. On this record, we determine that Petitioner has not established a reasonable likelihood of prevailing on either assertion.

We incorporate here our findings above regarding the teachings and disclosure of Rodgers.

1. Jakafi Label (Ex. 1004)

Jakafi Label provides prescribing information for JAKAFI (ruxolitinib). Ex. 1004, 1. Jakafi Label states "Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis" and provides information such as dosage and administration, contraindications, adverse reaction, and drug interactions. *Id.*

2. Shilling (Ex. 1005)

Shilling teaches that ruxolitinib is a "potent, selective inhibitor of Janus tyrosine kinase 1/2 and the first investigational drug of its class in phase III studies for the treatment of myelofibrosis." Ex. 1005, Abstract. Shilling discloses a study of the metabolism, excretion, and pharmacokinetics of ruxolitinib. *Id.* In its study, Shilling identifies two major metabolites of ruxolitinib: M18 (2-hydroxycyclopentyl ruxolitinib) and M16/M27 (3-hydroxycyclopentyl ruxolitinib). *Id.* at 2030.

3. Concert Backgrounder (Ex. 1006)

Concert Backgrounder discloses the product platform of CoNCERT Pharmaceuticals, Inc. Ex. 1006, 2. Concert Backgrounder explains the potential benefits of deuterium modification, including improved safety, better tolerability, and enhanced efficacy. *Id.* at 3. Concert Backgrounder states, however, that "the magnitude and nature of the deuterium benefit cannot be predicted *a priori*, [so] CoNCERT must test multiple compounds in a range of assays to identify those that are differentiated." *Id.*

4. Analysis

As an initial matter, Patent Owner challenges whether Petitioner has satisfied its initial burden of showing that Jakafi Label and Concert Backgrounder are printed publications. Prelim. Resp. 27–34. Because, as

explained below, we determine Petitioner has not shown a reasonable likelihood of prevailing, even assuming the references are printed publications, we need not address that issue for purposes of our decision.

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

We generally follow a two-part inquiry to determine whether a new chemical compound would have been obvious over particular prior art compounds. *Otsuka Pharm. Co. v. Sandoz, Inc*., 678 F.3d 1280, 1291–93 (Fed. Cir. 2012). First, we determine "whether a chemist of ordinary skill would have selected the asserted prior art compounds as lead compounds, or starting points, for further development efforts." *Id.* at 1291. Second, we analyze whether there was a reason to modify a lead compound to make the claimed compound with a reasonable expectation of success. *Id.* at 1292.

A lead compound is defined as "a compound in the prior art that would be most promising to modify in order to improve upon its . . . activity and obtain a compound with better activity." *Otsuka*, 678 F.3d at 1291 (citing *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd*., 492 F.3d 1350, 1357 (Fed. Cir. 2007)). Stated another way, "a lead compound is 'a natural

choice for further development efforts."' *Id.* (citing *Altana Pharma AG v. Teva Pharms. USA, Inc*., 566 F.3d 999, 1008 (Fed. Cir. 2009)). Importantly, the analysis of whether a person of ordinary skill in the art would have chosen the prior art compound as a lead compound "is guided by evidence of the compound's pertinent properties," including "positive attributes such as activity and potency," "adverse effects such as toxicity," and "other relevant characteristics in evidence." *Id.* at 1292.

Here, Petitioner does not expressly conduct a lead compound analysis. Instead, Petitioner asserts in Ground 1 that the claims are obvious because Jakafi Label teaches that ruxolitinib was a known, FDA-approved compound, and a person of ordinary skill in the art would have understood the compound to be particularly effective and relatively safe for use in a pharmaceutical composition. Pet. 29 (citing Ex. 1002 ¶ 67). Regarding Ground 3, Petitioner asserts that Rodgers teaches a genus of deuterated ruxolitinib compounds. Pet. 50–51.

For both Grounds, Petitioner contends that Shilling and Concert Backgrounder further provide a reason to make the claimed tetra- and octa-deuterated ruxolitinib analogs. Pet. 31–32, 50–53. Shilling teaches that oxidative metabolism occurs almost entirely on the cyclopentyl ring at Y^2 and Y^3. *Id.* at 31–32, 50–53 (citing Ex. 1002 ¶ 134). And Concert Backgrounder explains that deuterium substitution "has the potential to create new chemical entities with improved safety, tolerability, and efficacy" and that deuterium compounds useful for this technique are "based on drugs with known efficacy and safety that address clinically validated targets." *Id.* at 31, 51 (citing Ex. 1006, 2–3; Ex. 1002 ¶¶ 71–73, 136). According to Dr. Guengerich, Concert Backgrounder also teaches that compounds should be

selected that have known "metabolic hot spots" and should be deuterated at some or all of these metabolic hot spots. Ex. 1002 ¶ 136.

Thus, for Ground 1, Petitioner asserts that a person of ordinary skill in the art "would have been motivated to apply the techniques disclosed in the Concert Backgrounder to ruxolitinib because ruxolitinib was an FDA-approved drug with known efficacy and safety that addresses clinically validated targets as taught by [Jakafi Label], and ruxolitinib contained well-identified sites of *in vivo* oxidative metabolism, as shown by Shilling." Pet. 32 (citing Ex. 1002 ¶¶ 83–85). For Ground 3, Petitioner similarly asserts that a person of ordinary skill in the art "would have been motivated to apply the techniques disclosed in the Concert Backgrounder to ruxolitinib and/or the deuterated ruxolitinib of Rodgers because ruxolitinib was a claimed compound . . . in Rodgers and ruxolitinib contained well-identified sites of oxidative metabolism in *in vivo* metabolism, as shown in Shilling." Pet. 54 (citing Ex. 1002 ¶¶ 135–136).

In response, Patent Owner argues that Petitioner provides no reason why a person of ordinary skill in the art would have specifically chosen ruxolitinib as a lead compound over the thousands of FDA-approved drugs or the hundreds of compounds recited in Rodgers. Prelim. Resp. 35–36. Patent Owner further asserts that candidates for deuteration include drugs that "give rise to undesirable metabolites, are cleared from the bloodstream too quickly, are metabolically broken down in the intestines or liver before reaching the bloodstream, or interfere with the clearance of other medications a patient is taking." *Id.* at 36 (quoting Ex. 1013, 3). Because Petitioner does not identify anything in the cited references that raises any

such issue for ruxolitinib, Patent Owner contends that Petitioner's argument suffers from hindsight bias. *Id.*

Moreover, even assuming a person of ordinary skill in the art would have chosen ruxolitinib as a lead compound, Patent Owner argues that Petitioner does not identify a persuasive reason to modify ruxolitinib with deuterium. *Id.* at 38–39. Petitioner contends that a person of ordinary skill in the art would have been motivated to deuterate ruxolitinib "potentially to obtain superior ADME properties." Pet. 32. But Patent Owner notes that Petitioner has not identified any specific ADME property of ruxolitinib that would have motivated a person of ordinary skill in the art to improve it. Prelim. Resp. 39.

On this record, we are persuaded that Petitioner has not made a sufficient showing that a person of ordinary skill in the art would have chosen ruxolitinib as a lead compound or that there was a reason to deuterate ruxolitinib. Although Jakafi Label teaches that ruxolitinib is an FDA-approved drug and the combination of Rodgers and Shilling teaches ruxolitinib and its potential for treating myelofibrosis, we are not persuaded that Petitioner has shown sufficiently in either Ground that a person of ordinary skill in the art would have had a reason to choose ruxolitinib, as opposed to any other compound with known clinical efficacy. Under Petitioner's reasoning, *any* compound with known clinical efficacy would qualify as a lead compound. We, however, are not persuaded that that is sufficient, as it does not distinguish ruxolitinib "from the panoply of known compounds in the prior art." *Otsuka*, 678 F.3d at 1292.

Regardless, even assuming a person of ordinary skill in the art would have chosen ruxolitinib as a lead compound, we are not persuaded that

Petitioner has shown sufficiently that a skilled artisan would have had a reason to modify ruxolitinib by deuterium modification. Petitioner's declarant, Dr. Guengerich, explains that the potential clinical benefits of deuterium modification include:

> (i) improved safety by inhibiting the formation of toxic metabolites and reducing drug-drug interactions, (ii) better tolerability through reduction of overall dose and C_{max} (maximum plasma concentration of drug achieved), and (iii) enhanced efficacy by increasing bioavailability, AUC (area under the curve for drug), and C_{min} with minimal impact on C_{max}. Deuteration may also block elimination pathways enhancing the formation of active metabolites or toxic products.

Ex. 1002 ¶ 50 (citations omitted). Despite noting the clinical benefits of deuteration, Dr. Guengerich does not offer any evidence that a person of ordinary skill in the art would have understood that ruxolitinib was in need of any of those benefits. That is, neither Petitioner nor Dr. Guengerich cites any persuasive evidence that, for example, ruxolitinib metabolites were toxic, ruxolitinib was not well tolerated, or that ruxolitinib had poor bioavailability. Although Petitioner asserts that Concert Backgrounder suggests that compounds with metabolic hot spots should be chosen for deuteration, we are not persuaded that that alone is sufficient motivation for a person of ordinary skill in the art to modify ruxolitinib by deuterium substitution, particularly in light of Concert Backgrounder's statement that "the magnitude and nature of the deuterium benefit cannot be predicted *a priori*." Ex. 1006, 3.

Petitioner further asserts that "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed

compositions, creates a *prima facie* case of obviousness." Pet. 29–30 (quoting *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990)). Thus, because the deuterated ruxolitinib analogs differ from ruxolitinib only by the deuteration of the cyclopentyl ring, Petitioner argues that this alone is sufficient to establish a "*prima facie* rejection." Pet. 30–31. We disagree. Because we find Petitioner has not shown sufficiently that the prior art has given a reason or motivation to make deuterated ruxolitinib analogs, we are not persuaded by this argument, either.

Having considered the arguments and evidence, we determine Petitioner has not shown a reasonable likelihood of prevailing in its assertion that claims 1–15 of the '149 patent are unpatentable as obvious over the combinations of Jakafi Label, Shilling, and Concert Backgrounder or Rodgers, Shilling, and Concert Backgrounder.

III. PATENT OWNER'S PENDING MOTIONS

Patent Owner filed a Motion to Seal Exhibit 2019, which Patent Owner alleges contains confidential research and development information of Patent Owner. Paper 6. Patent Owner also filed an unopposed Motion for Modified Default Standing Protective Order. Paper 7. We did not rely on Exhibit 2019 in rendering this decision. Accordingly, we dismiss as moot the Motion to Seal and the Motion for Modified Default Standing Protective Order.

Patent Owner is authorized to file a motion to expunge Exhibit 2019 within thirty days of the date of this decision, or within thirty days of a decision on rehearing, if rehearing is requested. In the meantime, Exhibit 2019 shall remain provisionally sealed.

IV. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has not established a reasonable likelihood of prevailing on its assertion that claims 1–15 of the ’149 patent are unpatentable.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* as to all challenged claims of the ’149 patent, and no trial is instituted;

FURTHER ORDERED that Patent Owner’s Motion to Seal and Motion for Modified Default Standing Protective Order are *dismissed as moot*; and

FURTHER ORDERED that Patent Owner is authorized to file a motion to expunge Exhibit 2019 within thirty days of the date of this decision, or within thirty days of a decision on rehearing, if rehearing is requested.

PETITIONER:

Stephen Maebius
Michelle Simkin
smaebius@foley.com
msimkin@foley.com

PATENT OWNER:

Cynthia Lambert Hardman
Marta E. Delsignore
Sarah J. Fischer
chardman@goodwinlaw.com
mdelsignore@goodwinlaw.com
sfischer@goodwinlaw.com