UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

THORNE RESEARCH, INC.,
Petitioner,

v.

TRUSTEES OF DARTMOUTH COLLEGE,
Patent Owner.

Case IPR2021-00268

Patent 8,383,086

PRELIMINARY RESPONSE TO PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 8,383,086

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The Trustees of Dartmouth College ("Patent Owner") respectfully submit this Preliminary Response to the Petition seeking *inter partes* review of U.S. Patent No. 8,383,086 (Ex. 1001, "the '086 patent") filed by Thorne Research, Inc. ("Petitioner"). This Response is timely under 35 U.S.C. § 313 and 37 C.F.R. § 42.107 because it is within three months of the December 14, 2020 date of the Notice granting the Petition a filing date. Paper No. 3 (Notice of Filing Date) at 1.[1]

I. INTRODUCTION

Patent Owner respectfully submits that *inter partes* review of the '086 patent should not be instituted because Petitioner has failed to demonstrate that it has a reasonable likelihood of prevailing with respect to the challenged claim of the '086 patent.

First, two of Petitioner's three asserted references are not even prior art. The relied-upon portions of the '337 PCT Publication[2] and *Cell* article[3] regarding

[1] The three-month deadline is March, 14, 2021, which is a Sunday. This Response is timely filed on the next succeeding business day, March 15, 2021, under 35 U.S.C. § 21(b) and 37 C.F.R. § 42.107(a).

[2] International Publication No. WO 2005/077091 A2 ("the '337 PCT Publication") (Ex. 1007).

claim 2 of the ’086 patent are not “by another,” and thus these two references are not prior art under either pre-AIA § 102(a) or § 102(e).[4]

Moreover, Petitioner’s priority argument is based entirely on an unsupported theory that the ’086 patent priority claim is defective under the Paris Convention treaty. Tellingly, Petitioner cites no U.S. law or statute in support of its theory. The ’086 patent makes a proper priority claim to the ’701 Application under 35 U.S.C. § 120, the controlling U.S. statute, and Petitioner does not even attempt to argue otherwise. Thus, the *Cell* article is not prior art under pre-AIA § 102(b).

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[3] Bieganowski & Brenner, “Discoveries of Nicotinamide Riboside as a Nutrient and Conserved *NRK* Genes Establish a Preiss-Handler Independent Route to NAD^+ in Fungi and Humans,” 117 *Cell* 495 (May 14, 2004) (“the *Cell* article”) (Ex. 1008).

[4] The Petition refers to the ’337 PCT Publication and *Cell* article as “Brenner” (Ex. 1007) and “Bieganowski” (Ex. 1008), respectively. *See* Pet. at 30-33, 54. Because Patent Owner is submitting herewith declarations from both Dr. Brenner (Ex. 2002) and Dr. Bieganowski (Ex. 2003), Patent Owner will refer to the asserted references as the ’337 PCT Publication (Ex. 1007) and *Cell* article (Ex. 1008) to avoid confusion with the eponymous declarations.

Second, Grounds 1-2 based on Stamler fail to raise an issue of patentability. These Grounds are premised on an unsupported and improper application of collateral estoppel. Also, Stamler fails to disclose or suggest (1) "[a] pharmaceutical composition comprising nicotinamide riboside," (2) the nicotinamide riboside "in admixture with a carrier," or (3) the nicotinamide riboside "is isolated from a natural or synthetic source."

Indeed, the Petition's anticipation analysis fails because Petitioner concedes that these limitations are not explicitly disclosed by Stamler and does not argue inherency. The Petition's obviousness analysis likewise fails due to Petitioner's reliance on unsupported assertions and failure to address either all legal requirements for obviousness or all claim elements.

Third, the Board should exercise its discretion to deny institution because of the Petition's weak merits and because the challenged claim was previously ruled patentable by the Board and Federal Circuit and is also currently being challenged in a late-stage district court case.

For at least these reasons, the institution of an *inter partes* review of the '086 patent should be denied.

II. BACKGROUND

Charles M. Brenner, Ph.D. ("Dr. Brenner") is the sole named inventor of the '086 patent. Ex. 2002 ¶¶ 5, 10-14; '086 patent at (75). The claimed invention

stemmed from a nicotinamide riboside ("NR") research project ("NR research project") that Dr. Brenner led in late 2003 and early 2004 at Dartmouth Medical School. *See* Ex. 2002 ¶¶ 10-14. As part of the NR research project, Dr. Brenner established that NR is an unanticipated vitamin precursor of nicotinamide adenine dinucleotide ("NAD+"), and he identified and sequenced the gene that he ultimately named nicotinamide riboside kinase ("Nrk"). *Id.* ¶ 11. Dr. Brenner's laboratory research team included a postdoctoral fellow named Pawel Bieganowski Ph.D. ("Dr. Bieganowski"), who performed, at Dr. Brenner's direction, experiments and assays for identifying yeast and human genes that have Nrk activity. *Id.* ¶ 12; Ex. 2003 ¶ 6. Dr. Bieganowski did not have any role in any aspect of Dr. Brenner's inventions regarding therapeutic uses or compositions of NR. Ex. 2002 ¶ 13; Ex. 2003 ¶ 7.

As a result of the NR research project, Dartmouth filed U.S. Provisional Patent Application No. 60/543,347 ("the '347 Provisional") on February 10, 2004, and International Application No. PCT/US2005/004337 ("the '337 PCT Application") on February 9, 2005, which claimed priority to the '347 Provisional. *See* Ex. 1005; Ex. 1007; Ex. 2002 ¶¶ 6-7, 14. On August 25, 2005, the '337 PCT Application was published as the '337 PCT Publication, which Petitioner asserts in Ground 5 of this IPR as the "Brenner" reference. *See* Pet. at 32, 35; Ex. 1007; Ex. 2002 ¶ 7. The '347 Provisional and '337 PCT Publication both name Dr. Brenner

and Dr. Bieganowski as co-inventors, but the portions of the '337 PCT Publication relied upon by the Petition are solely the invention of Dr. Brenner, the named inventor of the challenged '086 patent. *See* Ex. 1005 at 3; Ex. 1007 at (75); Pet. at 32-33, 48-50; Ex. 2002 ¶¶ 6-7, 15-16; Ex. 2003 ¶¶ 5, 7.

Certain aspects of the NR research project were also included in the *Cell* article, which was published on May 14, 2004, and which Petitioner asserts in Grounds 3-4 of this IPR as the "Bieganowski" reference. *See* Pet. at 30, 35; Ex. 1008; Ex. 2002 ¶ 8. The *Cell* article names Dr. Brenner and Dr. Bieganowski as co-authors, but the portions of the *Cell* article relied upon by the Petition are solely the invention of Dr. Brenner, the named inventor of the challenged '086 patent. *See* Ex. 1008 at 495; Pet. at 42-48; Ex. 2002 ¶¶ 8, 17-19; Ex. 2003 ¶¶ 5, 7.

The '086 patent is directed to pharmaceutical compositions of NR formulated in admixture with a carrier for oral administration, wherein the NR is isolated from a natural or synthetic source. *See* '086 patent at claims 1-2. The '086 patent issued from a continuation application of U.S. Patent Application No. 11/912,400 ("the '400 Application"), which later issued as U.S. Patent No. 8,197,807 ("the '807 patent"). The '400 Application is a national stage entry of International Application No. PCT/US2006/015495 ("the '495 PCT"), which was published as International Publication No. WO 2006/116322 A2 and claims

priority to U.S. Patent Application No. 11/113,701 ("the '701 Application"). The '086 patent thus claims priority to the '701 Application. *See id.* at 1:7-13.

III. PETITIONER HAS NOT DEMONSTRATED "A REASONABLE LIKELIHOOD OF PREVAILING" UNDER 35 U.S.C. § 314(a) ON GROUNDS 3-5 BECAUSE THE '337 PCT AND *CELL* ARTICLE ARE NOT PRIOR ART

Under 35 U.S.C. § 314(a), an IPR may only be instituted where "the information presented in the petition … and any response … shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least one of the claims challenged in the petition." *See also* 37 C.F.R. § 42.108(c). The burden of showing that this statutory threshold has been met belongs to Petitioner. *See, e.g.*, Office Patent Trial Practice Guide, 77 Fed. Reg. 48756, 48756 (Aug. 14, 2012) ("The Board … may institute a trial where the petitioner establishes that the standards for instituting the requested trial are met … .").

Petitioner asserts Grounds 3-4 based on the *Cell* article and Ground 5 based on the '337 PCT Publication, but neither of these two references is prior art. First, the relied-upon portions of the *Cell* article and '337 PCT Publication are the sole invention of the named inventor of the '086 patent (Dr. Brenner), meaning that the *Cell* article and '337 PCT Publication are not prior art under 35 U.S.C. § 102(a) or § 102(e). Second, Petitioner's unsupported and inapplicable Paris Convention argument regarding the '086 patent's priority fails to establish the *Cell* article as prior art under 35 U.S.C. § 102(b).

Accordingly, Petitioner has failed to meet its burden of showing that there is a reasonable likelihood that it would prevail with respect to Grounds 3-5, and Petitioner's request for IPR should be denied.

A. The Asserted *Cell* Article and '337 PCT Publication Are Not Prior Art Under 35 U.S.C. § 102(a) or § 102(e)

Grounds 3-5 of the Petition are based on the *Cell* article and '337 PCT Publication. *See* Pet. at 35, 42-50. Petitioner asserts that the '337 PCT Publication is allegedly prior art to the '086 patent under pre-AIA § 102(a) or § 102(e). *See id.* at 32 n.7, 35.

To qualify as prior art under either § 102(a) or § 102(e), the portions of the reference relied upon as prior art must be "by another." That is, the relied-upon portions of the reference must be the invention of someone other than the inventor of the challenged '086 patent, *i.e.*, Dr. Brenner. Here, however, Dr. Brenner is the sole inventor of the relied-upon portions of the *Cell* article and '337 PCT Publication asserted by Petitioner, as confirmed by declaration testimony from both Dr. Brenner and the only other co-author or co-inventor named for those two references, *i.e.,* Dr. Bieganowski. The *Cell* article and the '337 PCT Publication are therefore not prior art under § 102(a) or § 102(e).

1. To Qualify as Prior Art Under § 102(a) or § 102(e), the Relied-Upon Portions Must Be "By Another"

Under Pre-AIA § 102, an inventor's own work is only prior art if it constitutes a statutory bar under § 102(b). *See Lacks Indus. v. McKechnie Vehicle Components USA, Inc.*, 322 F.3d 1335, 1346 (Fed. Cir. 2003) ("[I]t is 'well-settled' law that an inventor's own disclosure 'will not anticipate his later invention unless that prior work is such as to constitute a statutory bar under Section 102(b).'") (quoting Chisum on Patents § 3.08 [2][a] (1999)); *In re Katz*, 687 F.2d 450, 454 (C.C.P.A. 1982) ("[C]ertainly one's own invention, whatever the form of disclosure to the public, may not be prior art against oneself, absent a statutory bar [under § 102(b)]."") (internal quotation marks and citation omitted). An inventor's own work is thus not prior art under § 102(a) or § 102(e).

Under § 102(e), a claim is invalid only if "the invention was described in … an application for patent, published under section 122(b), ***by another*** filed in the United States before the invention by the applicant for patent." (Emphasis added). Thus, an applicant or patentee may "overcome a prior art reference under section 102(e)" by "establish[ing] that the relevant disclosure describes their own invention." *In re Costello*, 717 F.2d 1346, 1351 (Fed. Cir. 1983).

"[T]he fact that [a challenged patent] has named a different inventive entity than a [prior application] does not necessarily make that [reference application] prior art." *Applied Materials, Inc. v. Gemini Research Corp.*, 835 F.2d 279, 281

(Fed. Cir. 1987). Rather, "the relevant question is not whether the references list different inventors, but 'whether the portions of the reference relied on as prior art, and the subject matter of the claims in question, represent the work of a common inventive entity.'" *EmeraChem Holdings, LLC v. Volkswagen Grp. of Am., Inc.*, 859 F.3d 1341, 1345 (Fed. Cir. 2017) (quoting *Riverwood Int'l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1356 (Fed. Cir. 2003)). This analysis focuses on just "the portions of the reference relied on as prior art," not the reference as a whole. *Riverwood Int'l Corp.*, 324 F.3d at 1356.

As with § 102(e), one's own work is also not prior art under § 102(a). *Katz*, 687 F.2d at 454. Thus, a patentee may overcome a prior art reference under § 102(a) the same way as described above, *i.e.*, by establishing that the relied-upon portions of the reference describe their own invention. *See id.* at 455. Co-authoring an article does not make one an inventor of the subject matter disclosed therein. *See id.* ("[A]uthorship of an article by itself does not raise a presumption of inventorship with respect to the subject matter disclosed in the article.").

Where an inventor of a challenged patent is one of two co-inventors of an earlier application asserted under § 102(e), such as the '337 PCT Publication here, either a declaration by the inventor of the challenged patent that he conceived the relied-upon portions or a disclaimer declaration by the other named co-inventor of the application is sufficient to establish that the application is not "by another" and

is thus not prior art under § 102(e). *See, e.g.*, *In re DeBaun*, 687 F.2d 459, 463 (C.C.P.A. 1982) (finding inventor declaration sufficient); *In re Mathews*, 408 F.2d 1393, 1396 (C.C.P.A. 1969) (finding disclaimer declaration sufficient). Likewise, where an inventor of a challenged patent is one of two co-authors of a reference article asserted against the patent under § 102(a), such as the *Cell* article here, either a declaration by the inventor that he conceived the relied-upon portions of the article or a disclaimer declaration by the non-inventor co-author is sufficient to establish that the reference article is not by "others" and is thus not prior art under § 102(a). *See, e.g.*, *Katz*, 687 F.2d at 455-56 (finding an inventor declaration sufficient); *Ex Parte Hirschler*, 1952 Pat. App. LEXIS 55, at *7-10 (B.P.A.I. Jan. 31, 1952) (finding a disclaimer affidavit sufficient).

Unlike cases such as *Katz* though, where the burden is on an applicant "to establish that the subject disclosure was his original work, and his alone," 678 F.2d at 455, the burden here is on Petitioner to establish a reasonable likelihood that it would prevail in showing that the relied-upon portions of the *Cell* article and '337 PCT Publication were invented by Dr. Bieganowski rather than Dr. Brenner. *See Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (holding that, in an IPR, the burden of persuasion is on the petitioner and never shifts to the patentee).

2. Dr. Brenner Is the Sole Inventor of the Relied-Upon Subject Matter in the *Cell* Article and '337 PCT Publication

Dr. Brenner is the sole named inventor of the challenged '086 patent. '086 patent at (75); Ex. 2002 ¶¶ 1-5. Dr. Brenner is also the sole inventor of the portions of the *Cell* article and '337 PCT Publication upon which Petitioner relies, and therefore neither of those two references is "by another" as required by pre-AIA § 102(a) and § 102(e).

Dr. Brenner worked from July 1, 2003 to June 30, 2009 as a professor and researcher at Dartmouth Medical School, where he was the project leader and principal investigator of the NR research project. Ex. 2002 ¶ 10. As a part of that project, in late 2003, Dr. Brenner directed members of his team to conduct experiments and assays related to NR, and as a result, Dr. Brenner identified and named an Nrk gene and discovered sequences of the Nrk1 and Nrk2 genes in humans. *Id.* ¶ 11. One member of Dr. Brenner's research team was Dr. Bieganowski, who was at the time a postdoctoral fellow in molecular biology who performed, at Dr. Brenner's direction, experiments and assays for identifying yeast and human genes that have Nrk activity. *Id.* ¶ 12; Ex. 2003 ¶ 6.

Dr. Brenner was solely responsible for all aspects of the NR research project related to therapeutic uses and compositions of NR, including the pharmaceutical composition recited in claim 2 of the '086 patent. Ex. 2002 ¶ 13; *see also* Ex. 2003 ¶ 7. Dr. Bieganowski did not contribute to the invention recited in claim 2 of the

'086 patent or to any aspect of the NR research project regarding therapeutic uses or compositions of NR. Ex. 2002 ¶ 13; Ex. 2003 ¶ 7.

Certain aspects of the NR research project were disclosed in the '347 Provisional, which Dartmouth filed on February 20, 2004. Ex. 2002 ¶ 14; *see* Ex. 1005 at 2. Dartmouth later claimed priority to the '347 Provisional in the '337 PCT Application, which was later published as the '337 PCT Publication. *See* Ex. 1007; Pet. at 32; Ex. 2002 ¶¶ 6-7, 15; Ex. 2003 ¶¶ 5, 7. Certain results from the NR research project were also published in the *Cell* article. *See* Ex. 1008; Pet. at 30; Ex. 2002 ¶¶ 8, 14, 17-18; Ex. 2003 ¶¶ 5, 7.

The '347 Provisional and the '337 PCT Publication both name Dr. Brenner and Dr. Bieganowski as co-inventors. *See* Ex. 1005 at 3; Ex. 1007 at (75); Ex. 2002 ¶¶ 6-7; Ex. 2003 ¶ 5. However, the relied-upon portions of the '337 PCT Publication represent the invention of Dr. Brenner alone; Dr. Bieganowski was not the inventor of the subject matter in these relied-upon portions of the '337 PCT Publication. *See* Pet. at 32-33, 48-50; Ex. 2002 ¶¶ 15-16; Ex. 2003 ¶ 7.

The *Cell* article names Dr. Brenner and Dr. Bieganowski as co-authors. *See* Ex. 1008 at 495; Ex. 2002 ¶ 8; Ex. 2003 ¶ 5. However, the relied-upon portions of the *Cell* article represent the invention of Dr. Brenner alone; Dr. Bieganowski was not the inventor of the subject matter in these relied-upon portions of the *Cell* article. *See* Pet. at 42-48; Ex. 2002 ¶¶ 17-19; Ex. 2003 ¶ 7.

Patent Owner provides herewith unequivocal declarations from both Dr. Brenner and Dr. Bieganowski, who are the only two co-inventors of the '337 PCT Publication and the only two co-authors of the *Cell* article. *See* Ex. 2002; Ex. 2003. The two declarations describe the NR research project that led to the disclosures in the '337 PCT Publication and the *Cell* article, as well as each declarant's role and contributions. *See* Ex. 2002 ¶¶ 10-14; Ex. 2003 ¶¶ 6-7. The two declarations are consistent and make clear that the subject matter in both the '337 PCT Publication and the *Cell* article asserted in Grounds 3-5 is Dr. Brenner's own invention and not the invention of Dr. Bieganowski. *See* Ex. 2002 ¶¶ 12-19; Ex. 2003 ¶¶ 6-7. Further, Dr. Brenner's declaration is corroborated by the disclaimer declaration of Dr. Bieganowski, who is not a named inventor of the '086 patent. *See* Ex. 2003 ¶¶ 6-7.

Therefore, based on consistent and unequivocal testimony from the only two individuals involved with the asserted '337 PCT Publication and *Cell* article, those two references are not "by another" and are thus not prior art under pre-AIA § 102(a) or § 102(e). Although either an inventor declaration or a disclaimer declaration can suffice, here, Patent Owner provides both.

The Board has denied institution in previous cases where patent owners made such clear showings that the relied-upon portions of an asserted reference were the sole work of the inventor of the challenged patent. *See, e.g.*, *IronRidge*

Inc. v. Rillito River Solar, LLC, IPR2017-01681, Paper 11 at 10-12 (P.T.A.B. Jan. 9, 2018) (denying institution where inventor declaration supported position that an asserted reference described the inventor's own work and was not prior art). The same result should apply here, and the Petition should be denied.

B. The Asserted *Cell* Article Is Not Prior Art Under 35 U.S.C. § 102(b)

Grounds 3-4 of the Petition are based on the *Cell* article, which Petitioner asserts is prior art under pre-AIA § 102(b). *See* Pet. at 30 n.6, 35, 42-48. But a printed publication is only prior art under § 102(b) if it describes the invention "more than one year prior to" the '086 patent's priority date of April 25, 2005, *i.e.*, before April 25, 2004. The *Cell* article was not purportedly published until May 14, 2004 and is thus not prior art under § 102(b). *See id.* at 30 n.6; Ex. 1008 at 495.

Petitioner challenges the '086 patent's priority claim based solely on a Paris Convention argument that is both unsupported and inapplicable. *See* Pet. at 6-14. Instead, the '086 patent's priority claim meets the requirements set forth in the applicable statute, 35 U.S.C. § 120, and the Petition does not argue otherwise. Therefore, the Petition fails to raise a legitimate challenge to the '086 patent's priority claim and establish the *Cell* article as prior art under § 102(b).

1. Petitioner's Position on Priority Is Based on an Unsupported and Inapplicable Paris Convention Argument

The '086 patent claims priority through the '495 PCT to the '701 Application, filed April 25, 2005. *See* '086 patent at 1:7-13. Petitioner asserts, based on its unsupported Paris Convention argument, that the '086 patent cannot claim priority further back than the '495 PCT, filed April 20, 2006. *See* Pet. at 6-7. Petitioner's priority argument fails for several independent reasons: (1) it is premised entirely on non-self-executing treaties and is not supported by any controlling U.S. statute or case law, (2) the Paris Convention rule that Petitioner relies upon is enacted in 35 U.S.C. § 119 and is thus inapposite because the '086 patent's priority claim is governed instead by § 120, and (3) the Patent Cooperation Treaty ("PCT") provision that incorporates the Paris Convention rule relied upon by Petitioner also includes a relevant exception that applies here. The Petition's priority argument is therefore neither supported nor applicable to the '086 patent's priority claim.

a. Petitioner Relies Entirely on Treaties That Are Not Self-Executing and Fails to Cite Any U.S. Law

The Petition's argument regarding the '086 patent's priority claim is premised entirely on Article 4 of the Paris Convention for the Protection of

Industrial Property[5] ("Paris Convention"), as incorporated by Article 8 Section (2)(a) of the PCT.[6] *See* Pet. at 7-14. Specifically, Petitioner relies upon the rule in Paris Convention Article 4 Sections (C)(1)-(2) and (C)(4) stating that "[t]he periods of priority … shall be twelve months" "from the date of filing of the first application" and further setting forth the conditions under which "[a] subsequent application … shall be considered as the first application." Based on these treaty provisions, Petitioner asserts (i) that the '347 Provisional was allegedly the "first application," and (ii) because the '495 PCT was filed more than twelve months after the '347 Provisional, the '495 PCT allegedly cannot claim priority back to the '347 Provisional. *See* Pet. at 9, 13. Petitioner then asserts, without citation to any authority, that this alleged defect somehow infects claims of priority to subsequently-filed applications, such as the '701 Application. *See id.* at 13-14.

However, neither the Paris Convention nor the PCT is self-executing, and both treaties are thus only given effect to the extent they are implemented by U.S. statute. *See In re Rath*, 402 F.3d 1207, 1209-10 (Fed. Cir. 2005) ("[T]he Paris Convention is not a self-executing treaty and requires congressional implementation."); *Yasuko Kawai v. Metlestics*, 480 F.2d 880, 884 (C.C.P.A.

[5] Available at: https://wipolex.wipo.int/en/text/287556.

[6] Available at: https://wipolex.wipo.int/en/text/288637.

1973); *Actelion Pharm., Ltd. v. Matal*, 881 F.3d 1339, 1341 (Fed. Cir. 2018) (noting that "the [PCT] … was implemented in 35 U.S.C. § 351 *et seq*."). The Petition's priority argument fails for this reason alone, as it cites no support other than the Paris Convention treaty, as incorporated by the PCT, and neither of these two treaties is binding on the Board. Indeed, the Petition cites ***no U.S. statute or case law*** to support its priority argument. *See* Pet. at 6-14.

b. The Paris Convention Rule Relied Upon by Petitioner Is Enacted in 35 U.S.C. § 119, but the '086 Patent's Priority Claim Is Governed Instead by § 120

To the extent that Article 4 of the Paris Convention is implemented by U.S. statute, that U.S. statute is not applicable to the priority claim of the '086 patent. Article 4 of the Paris Convention, on which Petitioner's entire priority argument is predicated, was enacted by Congress in 35 U.S.C. § 119. *See Scimed Life Sys. v. Medtronic Vascular, Inc.*, 468 F. Supp. 2d 60, 67 n.6 (D.D.C. 2006) (recognizing that "Section 119 … [was] enacted in order to implement Article 4 of the Paris Convention" (citing *Vogel v. Jones*, 486 F.2d 1068, 1072 (C.C.P.A. 1973))). More specifically, Petitioner's priority argument relies on Paris Convention Article 4 Sections (C)(1)-(2) and (C)(4), and these provisions correspond with § 119 subsections (a) and (c), respectively.

As discussed above, Petitioner fails to cite or rely upon § 119 or any other U.S. statute. Regardless, Petitioner ***cannot*** rely upon § 119 because the portions of

that statute that correspond with Article 4 of the Paris Convention govern claims of ***foreign*** priority. *See* § 119(a), (c).

The Supreme Court and Federal Circuit make clear that § 119 applies only to claims of ***foreign*** priority. *See Return Mail, Inc. v. U.S. Postal Serv.*, 139 S. Ct. 1853, 1864 n.5 (2019) ("Section 119 discusses the effect of a patent application filed in a foreign country … on the patent-application process in the United States."); *In re Gosteli*, 872 F.2d 1008, 1010-11 (Fed. Cir. 1989). The actual language of the Paris Convention itself also shows that its Article 4 provisions apply only to claims of priority to ***foreign*** applications. *See, e.g.*, Paris Convention Art. 4(A)(1) ("Any person who has duly filed an application for a patent … *in one of the countries* of the Union … shall enjoy, for the purpose of filing *in the other countries*, a right of priority during the periods hereinafter fixed." (emphasis added)).

Here, however, the '086 patent's priority claim involves only ***domestic*** priority to United States applications. That is, each of the applications in the '086 patent's priority claim—*i.e.*, '400 Application, '495 PCT, and '701 Application—is either a U.S. patent application or an international (PCT) application designating the United States. None of those applications is a foreign application,[7] and the

[7] The '337 PCT Application and '347 Provisional are also not foreign applications.

Paris Convention rule enacted in § 119 thus does not apply to the '086 patent's priority claim.

Domestic priority, and therefore the '086 patent's priority claim, is instead governed by 35 U.S.C. § 120. *See* § 120 (providing conditions for priority to "an application previously filed in the United States, or as provided by section 363"); § 363 ("An international application designating the United States [*e.g.*, the '495 PCT] shall have the effect … of a national application for patent regularly filed in the [USPTO]."); § 365(c) (providing that "an international application designating the United States [*e.g.*, the '495 PCT] shall be entitled to the benefit of the filing date of a prior national application [*e.g.*, the '701 Application]" "[i]n accordance with the conditions and requirements of *section 120*" (emphasis added)). The distinction between § 119's application to foreign priority and § 120's application to domestic priority is clear. *See, e.g.*, *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1324 n.5 (Fed. Cir. 2008) (recognizing that "when a patent application is entitled to the benefit of the filing date of an earlier United States patent application," "[t]he statute that provides for that entitlement is 35 U.S.C. § 120," whereas "§ 119 … provides that an application is entitled to the benefit of the filing date of an earlier foreign application").

Unlike § 119, § 120 does not include the rule that Petitioner relies upon from Article 4 of the Paris Convention. *See generally* § 120 (imposing no requirement

of filing within 12 months of a "first" application). The Paris Convention rule is thus not imposed upon the '086 patent's priority claim under the applicable statute. Rather, § 120 only requires co-pendency between links of a priority chain. *See id.*

Therefore, Petitioner's priority argument fails because its argument is based entirely upon the Paris Convention rule, and that Paris Convention rule, as enacted in § 119, is wholly inapplicable to the '086 patent's priority claim.

c. The PCT Includes a Relevant Exception to the Paris Convention Rule Relied Upon by Petitioner

Even if the Paris Convention treaty and PCT were self-executing and constituted sufficient support before the Board, Petitioner's argument nonetheless fails because the PCT provision that incorporates Article 4 of the Paris Convention also includes a relevant exception that applies to the '495 PCT's priority claim to the '701 application. Article 8 Sections (1) and (2)(a) of the PCT incorporate Article 4 of the Paris Convention:

> (1) The international application may … claim[] the priority of one or more earlier applications filed in or for any country party to the Paris Convention … .
> (2)(a) Subject to the provisions of subparagraph (b), *the conditions for, and the effect of, any priority claim* declared under paragraph (1) *shall be as provided in Article 4 of the … Paris Convention* … .

(Emphasis added). The Petition cites the emphasized portion of the above-quoted PCT provision to support Petitioner's assertion that "Article 4 of the Paris

Convention governs priority claims made in applications filed under the [PCT]." Pet. at 7-8.

However, Petitioner's argument ignores that PCT Article 8 Section (2)(b) includes a relevant exception to the application of Paris Convention Article 4. *See* PCT Art. 8(2)(a) (stating that Article 4 of the Paris Convention provides conditions for PCT applications' priority claims "[s]ubject to the provisions of subparagraph [2](b)"). Specifically, PCT Article 8 Section (2)(b) provides that if "an international application" (*e.g.*, the '495 PCT) claims priority to a "national application[] filed in … a designated State" (*e.g.*, the '701 application), then "the conditions for, and the effect of, the priority claim in that State shall be governed by the national law of that State." Thus, U.S. law—not Article 4 of the Paris Convention—applies to the '495 PCT's claim of priority to the '701 application. And as discussed above, Petitioner's priority argument does not cite any U.S. law.

Therefore, even if the Board were to consider and apply only the Paris Convention treaty and PCT, Petitioner's priority argument nonetheless fails because Article 8 of the PCT includes a relevant exception under which the '495 PCT's priority claim to the '701 Application is exempted from the rule that Petitioner relies upon in Article 4 of the Paris Convention.

2. The ’086 Patent’s Priority Claim to the ’701 Application Meets the Requirements of 35 U.S.C. § 120

As discussed above, the ’086 patent’s priority claim to the ’701 Application is governed by 35 U.S.C. § 120. *See* ’086 patent at 1:7-13; 35 U.S.C. §§ 120, 363, 365(c). “Under § 120, a patent is entitled to the priority date of an earlier filed application if (1) the written description of the earlier filed application discloses the invention claimed in the later filed application sufficient to satisfy the requirements of § 112; (2) the applications have at least one common inventor; (3) the later application is filed before the issuance or abandonment of the earlier filed application; and (4) the later application contains a reference to the earlier filed application.” *In re NTP, Inc.*, 654 F.3d 1268, 1277 (Fed. Cir. 2011); *see also* 35 U.S.C. § 120. The ’086 patent’s priority claim, as well as the priority claims of the intermediate ’400 Application and ’495 PCT, satisfies each of these requirements of § 120.

First, each application in the priority chain from the ’086 patent back to the ’701 Application satisfies the requirements of § 112 regarding claim 2 of the ’086 patent. The specifications of the ’400 Application, ’495 PCT, and ’701 Application are all the same as the specification of the ’086 patent with respect to disclosure of the invention in claim 2 of the ’086 patent. For example, the Petition itself asserts that the subject matter of claim 2 of the ’086 patent is supported by the following disclosures in the ’086 patent’s specification: 2:62-3:3, 4:1-2, 4:14-

23, 8:57-62, 26:32-39, 26:64-27:4, 27:66-28:15, 28:49-29:37, 29:43-30:12, 32:54-33:2. *See* Pet. at 9-13. Those same exact disclosures are contained in the '400 Application, '495 PCT, and '701 Application. *See* Ex. 2004 ('807 patent, which issued from the '400 Application) at 3:3-11, 4:8-9, 4:21-31, 9:9-14, 27:7-14, 27:39-46, 28:41-57, 29:24-30:13, 30:19-56, 33:32-45; Ex. 2005 (international publication of the '495 PCT) at 3:23-31, 6:1-3, 6:15-27, 15:31-16:4, 53:25-32, 54:26-55:1, 57:1-17, 58:19-60:12, 60:18-61:23, 66:31-67:11; Ex. 2006 (file history of the '701 Application) at PO_DART086_2006-0011 to -0079 (specification, see specifically native pages thereof at 3:23-31, 6:1-3, 6:15-27, 15:31-16:4, 53:17-24, 54:19-27, 56:28-57:13, 58:17-60:11, 60:17-61:22, 66:29-67:9). Thus, the '701 Application and each application in the chain of priority back to the '701 Application satisfies § 112 for purposes of § 120.

Second, the '086 patent, '400 Application, '495 PCT, and '701 Application all name the same common inventor: Dr. Brenner. *See* '086 patent at (75); Ex. 2004 at (75); Ex. 2005 at (75); Ex. 2006 at 1.

Third, there was co-pendency among applications in the priority chain because each link in the priority chain from the '086 patent back to the '701 Application was co-pending with the preceding application in the chain. That is, the '086 patent was filed on April 12, 2012, before the issuance of the '400 Application as the '807 patent on June 12, 2012. *See* '086 patent at (22); Ex. 2004

at (45). And the ’400 Application is a national stage entry of the ’495 PCT, which was filed on April 20, 2006, before the abandonment of the ’701 Application on December 28, 2006. *See* Ex. 2004 at (22), (86); Ex. 2005 at (22); Ex. 2006 at 336-37.

Fourth, all applications in the chain specifically identify the earlier-filed applications to which priority is claimed. That is, the ’086 patent contains a reference to the ’701 Application and to the earlier-filed ’400 Application and ’495 PCT in the chain. *See* ’086 Patent at 1:7-13. Additionally, both the ’400 Application and ’495 PCT contain references to each earlier-filed application in the priority chain back to the ’701 Application. *See* Ex. 2004 at 1:11-13; Ex. 2005 at 1:7-9.

Thus, the ’086 patent and each other application in the priority chain back to the ’701 Application meets the requirements under § 120 for disclosure, common inventorship, co-pendency, and referencing. Indeed, Petitioner’s priority argument relies entirely upon the Paris Convention, as discussed above, and does not even assert that the ’086 patent’s priority claim fails to meet any of the requirements under § 120. Therefore, because § 120 is satisfied, the ’086 patent is entitled to the benefit of the ’701 Application’s filing date.

3. The *Cell* Article Is Not Prior Art Under § 102(b)

Because the '086 patent's priority claim to the '701 Application meets the requirements set forth in the applicable statute, § 120, the filing date of the '701 Application, *i.e.*, April 25, 2005, is the proper priority date. Therefore, the *Cell* article, which was purportedly published on May 14, 2004, was not published more than one year prior to the '086 patent's priority date and is not prior art under pre-AIA § 102(b). *See* Pet. at 30 n.6; Ex. 1008 at 495.

IV. PETITIONER HAS NOT DEMONSTRATED "A REASONABLE LIKELIHOOD OF PREVAILING" UNDER 35 U.S.C. § 314(a) ON GROUNDS 1-2 BECAUSE STAMLER DOES NOT DISCLOSE OR SUGGEST ALL LIMITATIONS OF CLAIM 2

As stated above, under 35 U.S.C. § 314(a), an *inter partes* review may only be instituted where "the information presented in the petition … and any response … shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least one of the claims challenged in the petition." *See also* 37 C.F.R. § 42.108(c). The burden of showing that this statutory threshold has been met belongs to Petitioner. *See, e.g.*, Office Patent Trial Practice Guide, 77 Fed. Reg. 48756, 48756 (Aug. 14, 2012) ("The Board … may institute a trial where the petitioner establishes that the standards for instituting the requested trial are met … .").

Grounds 1-2 are based on Stamler but fail to establish that Stamler discloses or suggests all limitations of the challenged claim 2 of the '086 patent. First,

Petitioner asserts a collateral estoppel argument in an attempt to dodge the requirement of showing that Stamler discloses or suggests the limitations incorporated into claim 2 via its dependency on claim 1, but this argument is unsupported and thus inapplicable. Next, Petitioner's anticipation analysis fails because Petitioner concedes that Stamler does not disclose several claim limitations and Petitioner does not argue that Stamler inherently discloses any of the missing limitations. Further, Petitioner's obviousness analysis likewise fails because the Petition relies on unsupported conclusory statements, does not address several obviousness requirements, and does not address all limitations of claim 2.

Accordingly, Petitioner has failed to meet its burden of showing that there is a reasonable likelihood that it would prevail with respect to Grounds 1-2, and Petitioner's request for IPR should be denied.

A. Claim Construction

In an IPR, claim terms "shall be construed using the same claim construction standard that would be used to construe the claim in a civil action … , including construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." 37 C.F.R. § 42.100(b); *see Immunex Corp. v. Sanofi-Aventis U.S. LLC*, 977 F.3d 1212, 1216 (Fed. Cir. 2020) (recognizing that "the Board applies the *Phillips* district-court claim construction standard" to IPRs

filed on or after November 13, 2018) (citations omitted); *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc). Accordingly, "[a]ny prior claim construction determination concerning a term of the claim in a civil action … that is timely made of record in the *inter partes* review proceeding will be considered." 37 C.F.R. § 42.100(b).

Additionally, the Board will consider any relevant prior claim construction determinations from previous IPRs. *See* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340, 51,344, 51,349 (Oct. 11, 2018) ("When construing claims in IPR … proceedings, the Office will take into account the prosecution history previously at the Office, including … prior AIA proceedings"; "[t]he PTAB … will consider any prior claim construction determinations from the PTAB … that are timely made of record to promote consistency.").

Claim terms of the '086 patent have already been construed in a previous IPR and in a co-pending civil action. The Board's prior claim constructions in *Elysium Health Inc. v. Trustees of Dartmouth College*, IPR2017-01795 ("the '1795 IPR"), are made of record here as Exhibit 1018 (Final Written Decision, Jan. 16, 2019). The prior claim construction determinations by the District Court for the District of Delaware ("District Court") in *ChromaDex, Inc., et al. v. Elysium*

Health, Inc., Case No. 18-cv-01434 (D. Del.), are made of record here as Exhibit 2007 (Claim Construction Order, Jan. 5, 2021). *See also* Ex. 2011 ¶ 4.

1. "pharmaceutical composition comprising nicotinamide riboside" (Claim 1)

The Board previously construed "pharmaceutical composition comprising nicotinamide riboside" as shown below.

Claim Term	Construction by the Board in the '1795 IPR
"pharmaceutical composition comprising nicotinamide riboside"	"a composition, including a food composition, which contains NR as an active agent in an amount effective for the treatment or prevention of a disease or condition associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis" *See* Ex. 1018 at 10-11.

In addition to the Board's construction in the '1795 IPR, the District Court construed the shorter phrase "pharmaceutical composition" to mean "a composition that can be used to improve or prolong the health or well-being of humans or other animals." *See* Ex. 2007 at 3. While Petitioner's arguments fail under either construction, Patent Owner applies the Board's prior construction from the '1795 IPR for purposes of this Preliminary Response.

Although the Petition purports also to adopt the Board's prior construction, Petitioner incorrectly identified the Board's prior construction, relying on only a portion of the Board's analysis and misstating the language used by the Board (*i.e.*, the Petitioner recited "the active agent," rather than "an active agent" as construed by the Board). *See* Pet. at 35-36; Ex. 1018 at 10-11.

2. "carrier" (Claim 1)

The Board previously construed the claim term "carrier" as shown below.

Claim Term	Construction by the Board in the '1795 IPR
"carrier"	"[A] liquid or solid filler, diluent, excipient, or solvent encapsulating material, [that] is involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be acceptable in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient." *See* Ex. 1018 at 14-15.

Patent Owner applies this construction for purposes of this Preliminary Response. The Petition adopts and observes this same construction. *See* Pet. at 35-36.

3. "is isolated from a natural or synthetic source" (Claim 2)

The Board previously construed the claim term "is isolated" as used in claim 2 of the '086 Patent as shown below.

Claim Term	Construction by the Board in the '1795 IPR
"is isolated [from a natural or synthetic source]"	"the nicotinamide riboside is separated or substantially free from at least some of the other components associated with the source of the molecule such that it constitutes at least 25% (w/w) of the composition" *See* Ex. 1018 at 14.

The District Court construed the phrase "the nicotinamide riboside is isolated from a natural or synthetic source" to mean "the nicotinamide riboside is isolated from a natural source or synthetic source and is not chemically synthesized." *See* Ex. 2007 at 2.[8] While Petitioner's arguments fail under either construction, Patent Owner applies the Board's prior construction from the '1795

[8] Plaintiffs, including Patent Owner, in the co-pending civil litigation proposed a different construction and disagreed with the District Court's construction because it adopted an improper waiver analysis. *See* Ex. 2008 at 41-52, 63-67; *see also* Ex. 2011 ¶ 5.

IPR for purposes of this Preliminary Response. Petitioner appears also to apply the Board's prior construction. *See* Pet. at 36-38.

B. Petitioner's Collateral Estoppel Argument Is Unsupported and Dartmouth Is Thus Not Precluded From Relying on Limitations of Claim 1 to Establish Patentability of Claim 2 Over Stamler

Petitioner, based on a conclusory misapplication of case law, attempts to avoid its burden to establish unpatentability. Petitioner argues throughout the Petition that Patent Owner is collaterally estopped from relying on the limitations of claim 1 to support the patentability of claim 2 allegedly due to the Board's prior determination in the '1795 IPR that claim 1 was unpatentable over Goldberger et al. and Goldberger and Tanner. *See* Pet. at 2, 22, 24, 39, 43, 49. The only support that Petitioner provides for its collateral estoppel argument are citations to two decisions: (1) *MaxLinear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1377 (Fed. Cir. 2018) (citing *Blonder-Tongue Labs., Inc. v. Univ. of Illinois Found.*, 402 U.S. 313 (1971)) and (2) *Alphatec Holdings, Inc. v. Nuvasive, Inc.*, IPR2019-00361, Paper 59, 23-27 (P.T.A.B. July 8, 2020). *Id.* As a threshold matter, Petitioner's argument fails because Petitioner does not make the requisite showing for collateral estoppel. And neither of the two decisions Petitioner cites stands for the proposition that Patent Owner is estopped from arguing that the references in this IPR—which are *different* than the references in the prior '1795 IPR—fail to teach the limitations of claim 1 from which the challenged claim 2 depends.

First, Petitioner fails to make the requisite showing for collateral estoppel to apply. "A party seeking to apply the doctrine of collateral estoppel based on a prior action must show that (1) the previous determination was necessary to the decision; (2) the identical issue was previously litigated; (3) the issue was actually decided in a decision that was final, valid, and on the merits; and (4) the party being precluded from relitigating the issue was adequately represented in the previous action. *United Access Techs., LLC v. CenturyTel Broadband Servs. LLC*, 778 F.3d 1327, 1331 (Fed. Cir. 2015) (citations omitted). Petitioner's collateral estoppel argument does not address these *United Access* factors and thus fails for that reason alone. *See* Pet. at 2, 22, 24, 39, 43, 49.

Second, Petitioner's collateral estoppel argument is not supported by *Alphatec*, which Petitioner cites twice without explanation. *See* Pet. at 21-22. Indeed, *Alphatec* is clearly distinguishable because there, the Board applied collateral estoppel in a later IPR that involved the ***same*** asserted prior art references from an earlier IPR. *See Alphatec*, Paper 59 at 23-27 (applying collateral estoppel where the asserted references included Frey and Michelson, which were the same basis on which related claims were found invalid in a prior IPR). The fact that the later IPR involved the ***same*** asserted references was critical to the Board's finding that three of the four *United Access* factors for collateral estoppel were satisfied. *See id.* at 26. Here, in contrast, Petitioner does not assert

the same references over which claim 1 was found invalid in the previous '1795 IPR, *i.e.*, Goldberger et al. and Goldberger and Tanner. Instead, Petitioner asserts ***different*** references. Nothing in *Alphatec* absolves Petitioner of its burden to establish that its newly asserted references disclose each and every limitation of the challenged claim, including the limitations of claim 1 that are incorporated into presumptively valid dependent claim 2. *See, e.g.*, 35 U.S.C. § 282 ("Each claim of a patent … shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim."); *K-Swiss Inc. v. Glide'n Lock GmbH*, 567 F. App'x 906, 911 (Fed. Cir. 2014) ("[I]n order to determine whether [the reference] anticipates dependent claims 3-5, which incorporate the limitations of claim 1, we must first determine whether [the reference] also anticipates independent claim 1).

Third, Petitioner's collateral estoppel argument is also not supported by *MaxLinear*, and Petitioner fails to establish otherwise. *See* Pet. at 2, 22, 24, 39, 43, 49. While *MaxLinear* and the case to which *MaxLinear* cites (*Blonder-Tongue*) relate to the general proposition that collateral estoppel can apply to the same patent owner in a subsequent proceeding against a different party, they do not stand for the overly restrictive application that Petitioner seeks here. *See MaxLinear*, 880 F.3d at 1377. Nothing in *MaxLinear* addresses whether collateral estoppel applies where a later patent challenger asserts different references in a

later IPR. Most importantly, *MaxLinear* does not absolve Petitioner of its obligation to establish that the asserted references teach every limitation of the challenged claims, including the limitations incorporated into a dependent claim from a previously-invalidated independent claim. Therefore, *MaxLinear* does not prevent Patent Owner from arguing that Stamler, which was not asserted in the previous '1795 IPR, fails to invalidate dependent claim 2 in this IPR because Stamler does not teach limitations incorporated into claim 2 from independent claim 1.

C. Ground 1: Petitioner Has Not Demonstrated a "Reasonable Likelihood of Prevailing" as to Anticipation of Claim 2 by Stamler

Petitioner fails to show that Stamler explicitly or inherently discloses every limitation of claim 2 of the '086 patent, as required for anticipation. *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997) ("To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently."). Specifically, Stamler does not disclose "[a] pharmaceutical composition comprising nicotinamide riboside," that the NR is "in admixture with a carrier," or that the NR "is isolated from a natural or synthetic source." '086 patent at claims 1-2. Petitioner concedes that Stamler does not explicitly disclose these limitations, *see* Pet. at 41, and Petitioner does not argue that Stamler discloses these limitations inherently.

Accordingly, Petitioner has failed to meet its burden of showing that there is a reasonable likelihood that it would prevail as to anticipation of claim 2 of the '086 patent by Stamler, and Petitioner's request for IPR should be denied.

1. Stamler Does Not Disclose "A pharmaceutical composition comprising nicotinamide riboside"

Claim 2 requires a "pharmaceutical composition comprising nicotinamide riboside," as recited in claim 1. '086 patent at claims 1-2. The Board previously construed this claimed phrase to mean "a composition, including a food composition, which contains NR as an active agent in an amount effective for the treatment or prevention of a disease or condition associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis." Ex. 1018 at 10-11. Petitioner fails to show that Stamler explicitly or inherently discloses this limitation as required for anticipation. *See Schreiber*, 128 F.3d at 1477.

Petitioner concedes that Stamler does not explicitly disclose a pharmaceutical composition comprising NR. *See* Pet. at 41 (admitting that "Stamler does not provide a specific example of a pharmaceutical composition comprising NR"); Ex. 1002 ¶ 81 (admitting that "Stamler does not specifically exemplify a pharmaceutical composition of [NR]"). While Petitioner fails to identify even a single composition in Stamler (*see* Pet. at 38-39), the only mention of ***any*** "composition" in Stamler is the inapplicable disclosure of a "topical composition" of ribavirin. Stamler at 15. The remainder of Stamler's teachings

are otherwise limited to methods of treatment with certain classes of compounds. *See* Stamler at 2-3. Petitioner does not establish that these methods disclose, much less enable, "[a] pharmaceutical composition comprising nicotinamide riboside" as required by claim 2.

Moreover, Petitioner does not argue that Stamler *inherently* discloses this limitation. *See* Pet. at 38-39; *see also* Pet. at 21 (alleging that the references in this IPR disclose the composition of claim 2 "explicitly," in contrast to the references asserted in the previous '1795 IPR, which relied upon inherency).

Accordingly, Petitioner has failed to establish that Stamler discloses the necessary element of "[a] pharmaceutical composition comprising nicotinamide riboside" as incorporated into challenged claim 2 from independent claim 1. Therefore, Petitioner has failed to show a reasonable likelihood that it will prevail in demonstrating that Stamler anticipates claim 2 of the '086 patent.

2. Stamler Does Not Disclose Nicotinamide Riboside "in admixture with a carrier"

Claim 2 requires that the claimed "pharmaceutical composition" comprises NR "in admixture with a carrier," as recited in claim 1. '086 patent at claims 1-2. The Board previously construed the claim term "carrier" to mean the following: "[A] liquid or solid filler, diluent, excipient, or solvent encapsulating material, [that] is involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must

be acceptable in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient." Ex. 1018 at 14-15. Petitioner fails to show that Stamler explicitly or inherently discloses this limitation as required for anticipation. *See Schreiber*, 128 F.3d at 1477.

Petitioner concedes that Stamler does not explicitly disclose the claimed "carrier." *See* Pet. at 41 (admitting that "Stamler does not expressly identify a carrier for oral administration"). Indeed, Petitioner fails to identify a single carrier in Stamler. *See id.* at 38-39. This is because there is no disclosure in Stamler of a "carrier," "filler," "diluent," "excipient," or "solvent." *See* Ex. 1018 at 14-15. Stamler does not disclose a pharmaceutical composition of NR, as discussed above, much less a carrier for inclusion in such a composition.

Moreover, Petitioner does not argue that Stamler *inherently* discloses this limitation. *See* Pet. at 38-39; *see also* Pet. at 21 (alleging that the references in this IPR disclose the composition of claim 2 "explicitly," in contrast to the references asserted in the previous '1795 IPR, which relied upon inherency).

Rather than argue that Stamler explicitly or inherently discloses NR "in admixture with a carrier," as required for anticipation, Petitioner instead relies on what "an ordinary artisan would have understood" and cites only a paragraph in Petitioner's expert declaration, which in turn cites only the '086 patent itself. *See* Pet. at 39 (citing Ex. 1002 ¶ 73); *cf. Schreiber*, 128 F.3d at 1477 (holding that

anticipation requires an explicit or inherent disclosure). Moreover, Petitioner attempts to cover up Stamler's deficiency by improperly conflating this claim limitation with the separate claim 1 limitation of "formulated for oral administration." *See* Ex. 1002 ¶ 78 (claim chart combines the limitation of "in admixture with a carrier" with the limitation of "formulated for oral administration" but only cites Stamler's disclosure of oral administration).

Accordingly, Petitioner has failed to establish that Stamler discloses the necessary element of NR "in admixture with a carrier" as incorporated into challenged claim 2 from independent claim 1. Therefore, Petitioner has failed to show a reasonable likelihood that it will prevail in demonstrating that Stamler anticipates claim 2 of the '086 patent.

3. Stamler Does Not Disclose a Pharmaceutical Composition Wherein the Nicotinamide Riboside "is isolated from a natural or synthetic source"

Claim 2 requires that the claimed "pharmaceutical composition" comprises NR that "is isolated from a natural or synthetic source." '086 patent at claim 2. The Board previously construed this limitation to mean that "the nicotinamide riboside is separated or substantially free from at least some of the other components associated with the source of the molecule such that it constitutes at least 25% (w/w) of the composition." *See* Ex. 1018 at 14. The District Court previously construed this limitation to mean that "the nicotinamide riboside is

isolated from a natural source or synthetic source and is not chemically synthesized." *See* Ex. 2007 at 2. Under either construction, Petitioner fails to show that Stamler explicitly or inherently discloses this limitation, as required for anticipation. *See Schreiber*, 128 F.3d at 1477.

Petitioner concedes that "Stamler … does not explicitly state that the NR is isolated." Pet. at 42. Petitioner instead attempts to rely only on Stamler's disclosure of NR and the sole statement in Stamler that "[t]he compounds specifically described above are available commercially or their synthesis is described in or obvious from the literature." *See id.* at 39-40 (citing Ex. 1006 at 4, 13).

Even if these vague statements could be read to disclose commercially available or synthetically produced NR, such disclosures do not satisfy the Board's prior construction of the "isolated" limitation of claim 2, which requires the NR to be "separated or substantially free from at least some of the other components associated with the source of the molecule such that it constitutes at least 25% (w/w) of the composition." *See* Ex. 1018 at 14. Petitioner has failed to point to any disclosure in Stamler that discloses either the "source" of the NR or any purity level associated with the NR. *See* Pet. at 40. Petitioner's failure to do so is not surprising because there are no such disclosures in Stamler. Instead, Petitioner resorts to an entirely different reference not included in Ground 1, *i.e.*, Ex. 1010

("Franchetti"), purportedly in an attempt to address the 25% purity requirement in the Board's construction. *See* Pet. at 40 (citing Franchetti and the discussion of Franchetti in the '086 patent). Petitioner's reliance on this separate reference is improper and fails to establish that Stamler discloses each and every limitation of claim 2, as required for anticipation. *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999) ("To anticipate, a single reference must teach every limitation of the claimed invention.").

For the same reasons, Petitioner's arguments regarding Stamler's limited disclosures would also fail under the District Court's construction of the "isolated" limitation. *See* Ex. 2007 at 2.

Moreover, Petitioner does not argue that Stamler *inherently* discloses this limitation. *See* Pet. at 40; *see also* Pet. at 21 (alleging that the references in this IPR disclose the composition of claim 2 "explicitly," in contrast to the references asserted in the previous '1795 IPR, which relied upon inherency).

Accordingly, Petitioner has failed to establish that Stamler discloses the necessary element that NR "is isolated from a natural or synthetic source" as recited in claim 2. Therefore, Petitioner has failed to show a reasonable likelihood that it will prevail in demonstrating that Stamler anticipates claim 2 of the '086 patent.

Institution of Ground 1 should be denied.

D. Ground 2: Petitioner Has Not Demonstrated A "Reasonable Likelihood of Prevailing" As To Obviousness of Claim 2 Over Stamler

Petitioner fails to show that Stamler discloses or suggests every limitation of claim 2 of the '086 patent, as required for obviousness. *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (holding that "obviousness requires a suggestion of all limitations in a claim" (citation omitted)). Specifically, Stamler does not disclose or suggest "[a] pharmaceutical composition comprising nicotinamide riboside," that the NR is "in admixture with a carrier," or that the NR "is isolated from a natural or synthetic source." '086 patent at claims 1-2. Petitioner's obviousness arguments for these limitations fail because they are conclusory, do not establish a motivation to modify Stamler, do not establish a reasonable expectation of success for the claimed pharmaceutical composition, do not enable the preparation of the claimed pharmaceutical composition, and do not address every element of the claim limitations.

Accordingly, Petitioner has failed to meet its burden of showing that there is a reasonable likelihood that it would prevail as to obviousness of claim 2 of the '086 patent over Stamler, and Petitioner's request for inter partes review should be denied.

1. Stamler Does Not Teach or Suggest (i) "A pharmaceutical composition comprising nicotinamide riboside" or (ii) Nicotinamide Riboside "in admixture with a carrier"

Petitioner concedes that Stamler does not disclose a pharmaceutical composition comprising NR. *See* Pet. at 41 (admitting that "Stamler does not provide a specific example of a pharmaceutical composition comprising NR"); Ex. 1002 ¶ 81 (admitting that "Stamler does not specifically exemplify a pharmaceutical composition of [NR]"). Petitioner also concedes that Stamler does not disclose the claimed "carrier." *See* Pet. at 41 (admitting that "Stamler does not expressly identify a carrier for oral administration"). Petitioner argues instead that these limitations are allegedly obvious "given Stamler's express suggestion of orally administering an inhibitor of glutathione-dependent formaldehyde dehydrogenase, such as NR," and "to facilitate administration of the NR to a patient." Pet. at 41. Petitioner argues that "formulating nicotinamide riboside for oral administration would have been well within the level of skill of the ordinary artisan." *Id.* at 41-42. This is the entirety of Petitioner's obviousness argument for these two limitations. *See id.*

Petitioner's obviousness argument fails because it is conclusory. "Rejections on obviousness grounds, in particular, cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *TQ*

Delta, LLC v. Cisco Sys., 942 F.3d 1352, 1359 (Fed. Cir. 2019) (internal quotation marks and citation omitted). In *TQ Delta*, the Federal Circuit reversed the finding of obviousness where the Board relied only on two paragraphs in the petition, which were in turn based on only the asserted reference (which did not expressly disclose a limitation) and two conclusory paragraphs of an expert declaration that, in turn, was based only on the asserted reference. *See id.* at 1361-63.

Here, similar to *TQ Delta*, Petitioner's obviousness argument for the "pharmaceutical composition" and "carrier" limitations comes from a single paragraph of the Petition and cites only Stamler, the challenged '086 patent itself, and three conclusory paragraphs of Petitioner's expert declaration that, in turn, only cite Stamler. *See* Pet. at 41-42 (citing Ex. 1006, Ex. 1001, and Ex. 1002 ¶¶ 80-83). Just as in *TQ Delta*, Stamler "provides no express discussion" of the claimed pharmaceutical composition and carrier, and Petitioner's expert "fails to identify any other evidence" besides Stamler and "instead offers only unsupported and conclusory statements." 942 F.3d at 1362. For example, Petitioner's expert offers conclusory statements that "a person of ordinary skill in the art would have found it obvious to provide [the claimed] composition," that there was "well-known use of carriers to facilitate administration of pharmaceutical compositions containing an active agent, such as nicotinamide riboside, to a patient," and that "formulating nicotinamide riboside for oral administration would have been well

within the level of skill of the ordinary artisan at the time of invention." Ex. 1002 ¶¶ 81-83. As in *TQ Delta*, however, these statements by Petitioner's expert "[are] unsupported by any evidence other than the disclosure of the invention in the [challenged patent]." 942 F.3d at 1362. Petitioner's obviousness argument thus fails because the Federal Circuit has "repeatedly recognized that conclusory expert testimony is inadequate to support an obviousness determination." *Id.* at 1359.

Petitioner's obviousness argument for these two limitations is also deficient because the Petition completely fails to state any motivation to modify Stamler. Obviousness based on only a single reference nonetheless requires a showing of motivation to modify the reference to meet the limitations of the claim. *See Arendi S.A.R.L. v. Apple Inc.*, 832 F.3d 1355, 1361 (Fed. Cir. 2016) ("[A] patent can be obvious in light of a single prior art reference if it would have been obvious to modify that reference to arrive at the patented invention."); *SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp.*, 225 F.3d 1349, 1356 (Fed. Cir. 2000) (holding that for "a single prior art reference" to render a claim obvious, "there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion"). The Petition does not mention a single motivation for modifying Stamler. *See* Pet. at 41-42. Moreover, Petitioner's conclusory expert testimony is insufficient to show a motivation to modify Stamler. *See* Ex. 1002 ¶¶ 80-83; *TQ Delta*, 942 F.3d at

1362-63 (holding that an expert's conclusory statements were inadequate to support the Board's factfinding regarding motivation to combine).

Petitioner's obviousness argument for these two limitations is also deficient because the Petition completely fails to address whether a person of ordinary skill in the art would have had a reasonable expectation of success of creating, based on Stamler, "[a] pharmaceutical composition comprising nicotinamide riboside in admixture with a carrier" as required by claim 2. *See* Pet. at 41-42; *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988) (holding that the "consistent criterion" for obviousness is "a reasonable likelihood of success, viewed in the light of the prior art."). Also, the Petition and Petitioner's expert report rely on disclosures in the challenged '086 patent to argue that the "pharmaceutical composition" and "carrier" limitations are obvious. *See* Pet. at 41-42; Ex. 1002 ¶ 82. However, "the expectation of success must be founded in the prior art, not in the applicant's disclosure." *Dow Chem.*, 837 F.2d at 473.

Regardless, there is no expectation of success based on Stamler because Stamler does not contain ***any*** teachings regarding pharmaceutical compositions or carriers. *See Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1365 (Fed. Cir. 2007) ("[T]o have a reasonable expectation of success, one must be motivated to do more than merely to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no

indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.") (internal quotation marks and citation omitted); *Grunenthal GMBH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1344-45 (Fed. Cir. 2019) (affirming finding of no reasonable expectation of success where the prior art reference "[did] not provide any guidance as to how the different solvents, varying temperatures, rates of agitation, or other variables used in polymorph screenings should be manipulated" and thus "there was little to no basis from which a POSA could expect a probability of success in producing Form A [of a polymorph]"). This is especially true here because claim 2 of the '086 patent is directed to a "pharmaceutical composition," and such chemical and pharmaceutical arts are unpredictable. *See, e.g., Eisai Co. Ltd. v. Dr. Reddy's Labs. Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008) (recognizing "chemical arts" as "unpredictable"); *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1292 (Fed. Cir. 2013) (recognizing that "formulation science carries with it a degree of unpredictability").

Finally, Petitioner's obviousness argument fails because Stamler does not enable the claimed "pharmaceutical composition comprising nicotinamide riboside in admixture with a carrier." "[I]n order to render an invention unpatentable for obviousness, the prior art must enable a person of ordinary skill to make and use the invention." *In re Kumar*, 418 F.3d 1361, 1368 (Fed. Cir. 2005) (citation omitted); *see, e.g.*, *Forest Labs., Inc. v. Ivax Pharm., Inc.*, 501 F.3d 1263, 1268-69

(Fed. Cir. 2007) (affirming judgment of no anticipation or obviousness by a prior art paper since the paper failed to provide an enabling disclosure of how to make the chemical composition it theorized). For example, in *Forest Laboratories*, the asserted reference was "not enabled with respect to [the claimed] (+)-citalopram" because the reference was "a pharmacology paper, not a chemical paper." 501 F.3d at 1268. That reference "describe[d] the effects of various enantiomers of particular drugs" and "it in effect [did] state that there is a (+)-enantiomer of citalopram, but it [did] not tell how to obtain it." *Id.* So, the "[asserted] reference, as a pharmacology paper, thus [did] not enable the preparation of the (+)-enantiomer of citalopram." *Id.* Similar to the asserted reference in *Forest Laboratories*, Stamler is a pharmacology-focused reference directed to methods of treatment, and it merely mentions NR as one compound in a class of potential compounds. Stamler does not tell how to obtain, and thus does not enable the preparation of, "[a] pharmaceutical composition comprising nicotinamide riboside" or NR "in admixture with a carrier," as required by claim 2 of the '086 patent.

Accordingly, Petitioner has failed to establish that Stamler teaches or suggests the necessary element of "[a] pharmaceutical composition comprising nicotinamide riboside" or NR "in admixture with a carrier" as incorporated into challenged claim 2 from independent claim 1. Therefore, Petitioner has failed to

show a reasonable likelihood that it will prevail in demonstrating that Stamler renders obvious claim 2 of the '086 patent.

2. Stamler Does Not Teach or Suggest a Pharmaceutical Composition Wherein the Nicotinamide Riboside "is isolated from a natural or synthetic source"

Petitioner concedes that Stamler does not disclose NR that "is isolated from a natural or synthetic source." *See* Pet. at 42 ("Stamler … does not explicitly state that the NR is isolated."). Petitioner's obviousness arguments for this element are limited to a single paragraph alleging only that (i) "synthesis of isolated NR was known in the art," (ii) "NR can be obtained commercially, isolated from natural sources using standard methods, or synthesized using established methods," and (iii) "it would have been well within the level of skill of the POSA to determine the level of isolation and purity for oral administration." *Id.* at 42. This is the entirety of Petitioner's obviousness argument for this limitation. *See id.*

Petitioner's argument fails to show that Stamler suggests NR "is isolated from a natural or synthetic source" as required by claim 2. Petitioner makes no attempt with any of its conclusory arguments to show how those arguments meet the claimed limitation under the Board's prior construction of this limitation. *See* Ex. 1018 at 14. For the same reasons, Petitioner's arguments regarding Stamler's limited disclosures would also fail under the District Court's construction of the "isolated" limitation. *See* Ex. 2007 at 2.

Petitioner's obviousness argument regarding this limitation also fails because it does not address every element of the limitation. To prove obviousness, Petitioner must demonstrate how each and every claim feature is shown or suggested by Stamler. *CFMT*, 349 F.3d at 1342 (holding that "obviousness requires a suggestion of all limitations in a claim" (citation omitted)); *see, e.g.*, *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1357 (Fed. Cir. 2012) (reversing finding of obviousness where claims required an amount of buffering agent but the prior art did not disclose or suggest that amount). The Petition, however, does not even argue that Stamler discloses or suggests "a natural or synthetic source" as required by claim 2 of the '086 patent. *See* Pet. at 42.

Moreover, Petitioner's obviousness argument regarding this limitation also fails for similar reasons as discussed above for the limitations of "[a] pharmaceutical composition comprising nicotinamide riboside" and NR "in admixture with a carrier." That is, Petitioner's obviousness argument for the limitation of "is isolated from a natural or synthetic source" fails because the argument and the expert testimony on which it relies are conclusory, as in *TQ Delta*, and rely only upon Stamler (which Petitioner admits does not disclose the limitation), the '086 patent itself, and a reference discussed in the '086 patent, *i.e.*, Ex. 1010 ("Franchetti"). *See* Pet. at 42 (citing Ex. 1002 ¶¶ 84-86; Ex. 1001; Ex. 1010); Ex. 1002 ¶¶ 84-86 (citing Ex. 1001; Ex. 1010); *TQ Delta*, 942 F.3d at 1359,

1361-63. Petitioner's obviousness argument for this limitation is also deficient because the Petition fails completely to state any motivation to modify Stamler or address any reasonable expectation of success. *See* Pet. at 42; *Dow Chem.*, 837 F.2d at 473 ("The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. … Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure." (citations omitted)); *Arendi*, 832 F.3d at 1361 (holding that single-reference obviousness nonetheless requires a showing of motivation to modify the reference to meet the claim limitations).

Accordingly, Petitioner has failed to establish that Stamler teaches or suggests the necessary element that NR "is isolated from a natural or synthetic source" as recited in claim 2. Therefore, Petitioner has failed to show a reasonable likelihood that it will prevail in demonstrating that Stamler renders obvious claim 2 of the '086 patent.

Institution of Ground 2 should be denied.

V. THE BOARD SHOULD EXERCISE ITS DISCRETION UNDER 35 U.S.C. § 314(a) TO DECLINE TO INSTITUTE REVIEW

The Board has discretion to deny institution of an IPR based on a holistic view of several non-exclusive sets of considerations related to the treatment of a

challenged patent in previous IPR proceedings and parallel district court cases, as well as consideration of a petition's merit. Here, based on a balanced assessment of all relevant circumstances, the Board should exercise its discretion to deny institution based on the weakness of the Petition's merits and based on a prior IPR and a co-pending late-stage district court case, which include challenges to the same patent and claim, as well as substantially similar art and arguments.

A. The Board Has Discretion to Deny Institution Based on a Prior IPR Proceeding, Art and Arguments Previously Before the Office, a Parallel District Court Case, and a Petition's Weak Merits

The Board has discretion to deny institution of an IPR under 35 U.S.C. § 314(a). *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1356, 1351 (2018) (holding that "§ 314(a) invests the Director with discretion on the question *whether* to institute review" (emphasis in original)); *Mylan Labs. Ltd. v. Janssen Pharm., N.V.*, --- F.3d ---, 2021 WL 936345, at *5 (Fed. Cir. Mar. 12, 2021) ("The Director is permitted, but never compelled, to institute an IPR. And no petitioner has a right to such institution. For example, the Director is free … to determine that for reasons of administrative efficiency an IPR will not be instituted … ."); *see also* 37 C.F.R. § 42.4(a). This discretion is informed by § 316(b), which requires consideration of "the efficient administration of the Office, and the ability of the Office to timely

complete [instituted] proceedings." *See* Patent Trial and Appeal Board Consolidated Trial Practice Guide November 2019 ("TPG")[9] at 56.

In deciding whether to institute, the Board takes into account various considerations. *See* TPG at 55-63. Such considerations include whether a petition is a "'follow-on' petition[] challenging the same patent as challenged previously in an IPR." TPB at 56. For this, the Board may consider the non-exclusive *General Plastic* factors, including the finite resources of the Board and whether a subsequent petition was filed after the patent owner's response and the Board's decision in a prior IPR. *Id.* at 56-57 (citing *General Plastic Indus. Co. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19 at 15-16 (P.T.A.B. Sept. 6, 2017) (precedential)).

The Board will also consider a two-part framework under 35 U.S.C. § 325(d), which first looks at "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 second, if either of those conditions is met, considers "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-

[9] Available at: https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf.

01469, Paper 6 at 8 (P.T.A.B. Feb. 13, 2020) (precedential). This analysis applies to situations where similar art or arguments were before the Office during a previous IPR. *See id.* at 10 (precedential). For the first part of the test, the Board may consider non-exclusive *Becton Dickinson* factors regarding "the similarities" between and "cumulative nature of" the asserted art and the previously-presented prior art, and "the extent of the overlap between the arguments made [previously] and the manner in which petitioner relies on the prior art [or patent owner distinguishes the prior art]." *See id.* at 9-10 (precedential) (citing *Becton Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17-18 (P.T.A.B. Dec. 15, 2017) (precedential in relevant part)).

The *General Plastic* factors and *Becton Dickinson* factors are not exclusive though, and the Board may also deny institution based on "the advanced state of a parallel district court proceeding" that involves the same patent. *See* TPG at 58, 62 (citing *NHK Spring Co. v. Intri-Plex Techs., Inc.*, IPR2018-00752, Paper 8 (P.T.A.B. Sept. 12, 2018) (precedential)). In deciding whether "efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in [a] parallel proceeding," the Board's "holistic view" may include consideration of the *Fintiv* factors. *Apple, Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 at 5-6 (P.T.A.B. Mar. 20, 2020) (precedential). These *Fintiv* factors include "whether the court granted a stay or evidence exists that one may

be granted if a proceeding is instituted," "proximity of the court's trial date to the Board's projected statutory deadline for a final written decision," "investment in the parallel proceeding by the court and the parties," "overlap between issues raised in the petition and in the parallel proceeding," and "other circumstances that impact the Board's exercise of discretion, including the merits." *Id.*

Notably, the considerations described above are not limited to subsequent petitions by the same petitioner or parallel district court cases involving the at-issue petitioner. *See* TPG at 57 n.1, 58; *NetApp Inc. v. Realtime Data LLC*, IPR2017-01195, Paper 9 at 10 (P.T.A.B. Oct. 12, 2017) (denying institution where "a different petitioner filed a petition challenging a patent that had been challenged already by previous petitions," as the Board's discretion under § 314(a) "is not limited to situations where the same party files multiple petitions"); *Unified Patents, Inc. v. PersonalWeb Techs., LLC*, IPR2014-00702, Paper 13 at 6-9 (P.T.A.B. July 24, 2014) (precedential) (denying institution under § 325(d) based on previous IPRs by different petitioners); *Mylan Labs. Ltd. v. Janssen Pharm. NV*, IPR2020-00440, Paper 17 at 13-25 (P.T.A.B. Sept. 16, 2020) (denying institution based in part on parallel litigation that did not involve the petitioner).

Additionally, the Board may exercise its discretion to deny institution based on a petition's weak merits. *See* TPG at 58 (stating that exercising discretion to deny institution is "part of a balanced assessment of all relevant circumstances in

the case, *including the merits*" (emphasis added)). "[W]eaker merits may favor exercising discretion to deny institution." *TCO AS v. NCS Multistage Inc.*, PGR2020-0007, Paper 16 at 18 (P.T.A.B. Feb. 18, 2021) (citing *Fintiv*, IPR2020-00019, Paper 11 at 15 (precedential)). For example, in *TCO AS*, the Board held that "the weakness of the merits of Petitioner's petition," along with an overlap of parallel proceedings, "outweigh[ed] the factors in favor of exercising discretion to institute." PGR2020-0007, Paper 16 at 23.

B. Institution Should Be Denied Based on the Prior '1795 IPR, the District Court Case in Delaware, and the Petition's Weak Merits

The Board should exercise its discretion to deny institution of the Petition based on the considerations below for purposes of efficiency, fairness, and timing.

Although Petitioner goes to great pains to argue against discretionary denial, a closer evaluation reveals that Petitioner's arguments are nothing more than conclusory assertions that certain factors weigh in its favor, while conveniently ignoring the weakness of its grounds. *See* TPG at 58 (stating that exercising discretion to deny institution is "part of a balanced assessment of all relevant circumstances in the case, including the merits"). At the outset, Petitioner incorrectly states that *Fintiv* does not apply (*see* Pet. at 17 n.4) in the face of clear precedent that discretionary denial considerations, including the *Fintiv* factors, are not limited to instances where Petitioner is the same party involved in a prior IPR or parallel district court proceeding. *See, e.g.*, TPG at 57 n.1, 58; *NetApp*,

IPR2017-01195, Paper 9 at 10; *Unified Patents*, IPR2014-00702, Paper 13 at 6-9 (precedential); *Mylan Labs.*, IPR2020-00440, Paper 17 at 13-25.

There is no dispute that the Petition is a follow-on challenge of claim 2 of the ’086 patent. This same patent and claim were previously challenged and upheld as patentable in the ’1795 IPR, which was affirmed by the Federal Circuit. *See* Ex. 1018 at 3; Ex. 1004 at 1-2. The Board’s final written decision and the Federal Circuit’s affirmance were issued in January 2019 and March 2020, respectively, well before the present Petition was filed in December 2020, so the Petitioner has the benefit of Patent Owner’s filings and the Board’s decisions in the prior ’1795 IPR and related appeal. *See* Ex. 1018 at 1, Ex. 1004 at 2, Pet. at 56.

Notwithstanding the availability of the record from the ’1795 IPR, the prior art and arguments in the Petition here are substantially the same as those considered and rejected by the Board in the previous ’1795 IPR. Given that the *Cell* article and ’337 PCT Publication are not prior art to the ’086 patent, the only “new” prior art asserted in the Petition here is the Stamler reference, which at most vaguely suggests the presence of NR without disclosing the other elements of the challenged claim. *See supra* Section IV.C-D. In the previous ’1795 IPR, the Board found that the asserted prior art *did not* disclose NR that “is isolated from a natural or synthetic source,” as required by claim 2, but *did* include the other elements of the challenged claims, including the incorporated limitations of

independent claim 1. *See* Ex. 1018 at 16, 32. Just like the references asserted in the '1795 IPR, Stamler also does not disclose NR that "is isolated from a natural or synthetic source" as recited in claim 2. *See supra* Sections IV.C.3, IV.D.2. Here, however, Stamler further fails to disclose the incorporated limitations from claim 1, including the "pharmaceutical composition" and "carrier" limitations. *See supra* Sections IV.C.1-2, IV.D.1. The Stamler reference asserted here is thus no better, and is in fact worse, than the references asserted in the earlier '1795 IPR. What is apparent from the Petition's thin arguments is that Petitioner is attempting to use Stamler, coupled with an incorrect collateral estoppel argument (*see supra* Section IV.B), to try to plug the holes in the '1795 IPR prior art. Petitioner's strategy is contrary to the Board's express directive that "using our decisions as a roadmap, until a ground is found that results in the grant of review … is unfair to patent owners and is an inefficient use of the *inter partes* review process." *General Plastic Indus.*, IPR2016-01357, Paper 19 at 17-18 (precedential).

Petitioner's discretionary denial arguments also fail to properly apply the Board's two-part framework under *Advanced Bionics*. With respect to the *Cell* article, although it is not prior art, Petitioner's argument that "the first part of the Board's two-part framework is not satisfied" is demonstrably false. Pet. at 19. Petitioner omitted the fact that the *Cell* article was submitted to the Office in an IDS and marked as considered by the Examiner, thereby satisfying the first part of

the framework. Ex. 1004 at 179; *Advanced Bionics*, IPR2019-01469, Paper 6 at 7-8 (precedential). Petitioner's discretionary denial argument then does not address the second part of the Board's framework and is thus facially defective, and the Board should deny institution. *See* Pet. at 19 (stating "the second part need not be reached"); *Advanced Bionics*, IPR2019-01469, Paper 6 at 8-9 (precedential) ("If a condition in the first part of the framework is satisfied and the petitioner fails to make a showing of material error, the Director generally will exercise discretion not to institute *inter partes* review").

The Board should also deny institution because the '086 patent is being challenged in a parallel district court case—*i.e.*, *ChromaDex, Inc., et al. v. Elysium Health, Inc.*, Case No. 18-cv-01434 (D. Del.) ("the District Court case")—that has a trial scheduled prior to the Board's statutory deadline for a final written decision. The District Court case includes a challenge to the validity of the same patent and claim challenged in the present Petition. *See* Ex. 2011 ¶ 6. Trial is scheduled to begin in the District Court case on September 27, 2021. *See id.* ¶ 7-8; Ex. 2009 at PO_DART086_2009-0003; Ex. 2010. In contrast, if an IPR were instituted here, the projected statutory deadline for a final written decision would be June 15, 2022, over eight months after the District Court's trial date. *See* 35 U.S.C. §§ 314(b), 316(a)(11). The District Court case is not stayed. *See* Ex. 2011 ¶ 9. Also, Petitioner provides no evidence of a potential stay, and a stay is unlikely due to the

advanced stage of the District Court case and the long delay between its scheduled trial and the projected statutory deadline for the Petition.

Conducting a parallel review of a patent that the Board and the Federal Circuit have already reviewed from a prior IPR that involved similar art and arguments, and which is also currently being challenged in late-stage district court litigation, would be an inefficient use of the Board's resources, and the Petition should therefore by denied.

The Petition's weak merits also support denial. Two of the three references asserted in the Petition are not even prior art, and those references account for three of the five asserted Grounds. *See supra* Section III. And in an attempt to qualify one of those references as prior art, the Petition sets forth a priority argument based entirely on an unsupported and inapplicable Paris Convention theory that ignores U.S. law. *Id.* For the single asserted reference that qualifies as prior art, Stamler, the Petition relies on an unsupported collateral estoppel theory, concedes that Stamler does not disclose several claim limitations, and fails to address the basic requisites to show obviousness. *See supra* Section IV.B-D.

For each of these reasons, Patent Owner respectfully requests that the Board exercise its discretion and deny institution.

VI. CONCLUSION

For the foregoing reasons, there is not a reasonable likelihood of Petitioner prevailing with respect to the challenged claim of the '086 patent. Accordingly, the Petition should be denied under 35 U.S.C. § 314(a).

Respectfully submitted,

Date: March 15, 2021

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CERTIFICATION UNDER 37 C.F.R. §42.24

Under the provisions of 37 C.F.R. §42.24, the undersigned hereby certifies that the foregoing document contains 13,879 words, and thus complies with the word-count limits of 37 C.F.R. § 42.24.

Date: March 15, 2021

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), the undersigned hereby certifies that a copy of the foregoing PRELIMINARY RESPONSE TO PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 8,383,086 was served on March 15, 2021 by filing this document through the Patent Trial and Appeal Board End to End as well as by delivering a copy via the delivery method indicated to the attorneys of record for the Petitioner as follows:

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