

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BTC CORPORATION,
Petitioner,

v.

TG BIOTECH CO., LTD.,
Patent Owner.

IPR2022-00998
Patent 8,357,786 B2

Before ULRIKE W. JENKS, JAMES A. WORTH, and
AVELYN M. ROSS, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314, 37 C.F.R. § 42.4

I. INTRODUCTION

A. *Background*

BTC Corporation (“Petitioner”) filed a Petition for an *inter partes* review of claims 1–13 (“the challenged claims”) of U.S. Patent No. 8,357,786 B2 (Ex. 1001, “the ’786 patent”). Paper 2 (“Pet.”). TG Biotech Co., Ltd. (“Patent Owner”) filed a Patent Owner Preliminary Response to the Petition. Paper 6 (“Prelim. Resp.”).

B. *Summary of the Institution Decision*

For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Because Petitioner has demonstrated a reasonable likelihood that at least one claim of the ’786 patent is unpatentable, we institute an *inter partes* review of all challenged claims based on the grounds raised in the Petition. *See SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018); *see also* Guidance on the Impact of SAS on AIA Trial Proceedings (April 26, 2018), *available at* <https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial> (“Guidance”).

Our findings of fact, conclusions of law, and reasoning discussed below are based on the evidentiary record developed thus far, and made for the sole purpose of determining whether the Petition meets the threshold for initiating review. This decision to institute trial is not a final decision as to the patentability of any challenged claim or the construction of any claim limitation. Any final decision will be based on the full record developed during trial.

C. *Real Parties in Interest*

Petitioner identifies itself, BTC Corporation, as the real party-in-interest. Pet. 4. Patent Owner identifies itself, TG Biotech Co., Ltd., as the real party-in-interest. Paper 4, 2.

D. *Related Matters*

Petitioner states that “[t]here are no judicial or administrative matters in the United States that would affect or be affected by a decision in this proceeding.” Pet. 4. Patent Owner agrees. Paper 4, 2.

E. *Asserted Grounds of Unpatentability*

Petitioner challenges the patentability of claims 1–13 of the '786 patent on the following grounds:

Claim(s) Challenged	35 U.S.C. § ¹	Reference(s)/Basis
1–13	103	Kim 460, ² Razmovski ³
1–13 ⁴	103	Kim 460, Kang, ⁵ Baek ⁶
8–10, 12, 13	103	WO 178, ⁷ Razmovski
1–13	103	WO 178, Kang
8, 9, 12	103	Huh ⁸

Pet. 6. In support of its patentability challenge, Petitioner relies on, *inter alia*, the Declaration of Neal Davies, Ph.D. Ex. 1003.

¹ The Leahy-Smith America Invents Act (“AIA”) included revisions to 35 U.S.C. § 103 that became effective on March 16, 2013. Because the '786 patent issued from an application filed before March 16, 2013, we apply the pre-AIA versions of the statutory bases for unpatentability.

² US Patent No. 5,776,460, issued July 7, 1998 (Ex. 1005). Both Petitioner and Patent Owner refer to this reference as “Kim 460;” thus, we shall do the same.

³ Razmovski-Naumovski, V., et al., *Chemistry and pharmacology of Gynostemma pentaphyllum*, PHYTOCHEMISTRY REVIEWS 4:197–219 (2005) (Ex. 1007). Both Petitioner and Patent Owner refer to this reference as “Razmovski;” thus, we shall do the same.

⁴ In the “Grounds of Challenge” table, it appears that Petitioner inadvertently switched Ground B with Ground C. *See* Pet. 6, 41, 47.

⁵ Korean Pub. No. 10-2006-0063041, published June 12, 2006. We refer to the English-language translation of Kang provided by Petitioner (Ex. 1010).

⁶ Korean Pub. No. 10-2007-0109282, published November 15, 2007. We refer to the English-language translation of Baek provided by Petitioner (Ex. 1008).

⁷ International Pub. No. WO 2008/140178 A1, published November 20, 2008 (Ex. 1006). Both Petitioner and Patent Owner refer to this reference as “WO 178;” thus, we shall do the same.

⁸ US Patent Pub. No. 2006/0246163 A1, published November 2, 2006 (Ex. 1020).

F. *The '786 patent (Ex. 1001)*

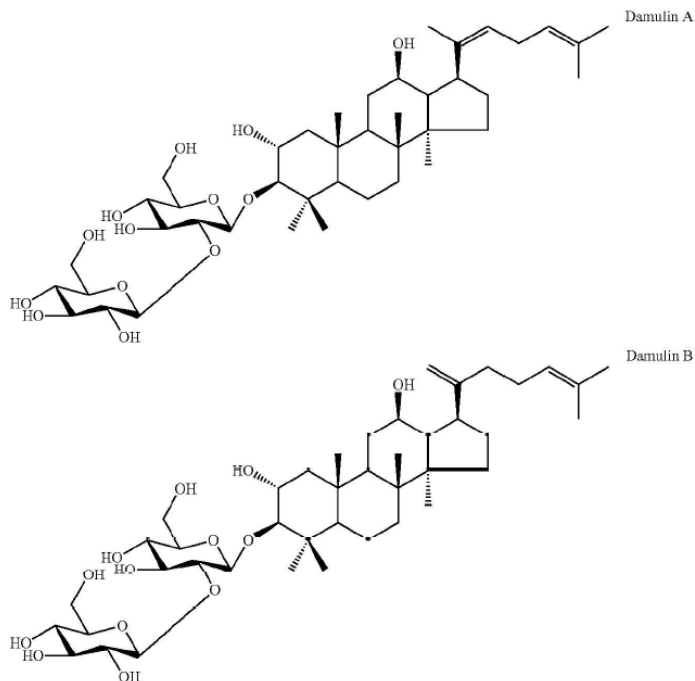
The '786 patent is titled “Method for Preparing *Gynostemma Pentaphyllum* Extract with Increasing Damulin A and Damulin B Contents, and Pharmaceutical Compositions of the Same for Treating Metabolic Disease.” Ex. 1001, code (54). The '786 patent “relates to a method for preparing a novel composition-containing *Gynostemma pentaphyllum* extract, in which a *Gynostemma pentaphyllum* extract is treated with high temperature and high pressure, thereby increasing contents of damulin A and damulin B (active ingredients for AMPK [(AMP-activated protein kinase)] activation)” and “a method for using a novel *Gynostemma pentaphyllum* extract with a novel composition having increased contents of damulin A and damulin B to efficiently treat and improve metabolic syndrome[s] including obesity, diabetes, hyperlipidaemia, or the like.” *Id.* at 1:19–29. The '786 patent explains that AMPK is a heterotrimer protein that exists generally in muscle cells in abundance and “plays an important role in appetite regulation, weight regulation, blood glucose regulation, and blood lipid metabolism regulation, or the like.” *Id.* at 1:31–38. The '786 patent further explains that *Gynostemma pentaphyllum* is a perennial vine of the family Cucurbitaceae and an extract tea derived from such has been used for a variety of ailments, such as constipation, diarrhea, asthma, and bronchitis, and provided health benefits, including restoring internal organ functions, maintaining healthy skin, and relieving pain and ulcers from stress. *Id.* at 2:27–41. It is known that “a *Gynostemma pentaphyllum* extract can improve metabolic syndrome, including insulin resistance, obesity, and hyperlipidaemia, by increasing the activity of AMP-activated protein kinase (AMPK).” *Id.* at 2:42–45. The '786 patent purports to have found, “through the analysis of the components of the *Gynostemma pentaphyllum* extract”

“that damulin A and damulin B included in the *Gynostemma pentaphyllum* extract are influential in the activity of AMPK” and provides a “novel *Gynostemma pentaphyllum* extract with a novel composition having increased contents of damulin A and damulin B” that “was determined to have a better capability for phosphorylation and enzymatic activation of AMPK, than a conventional *Gynostemma pentaphyllum* extract.” *Id.* at 2:46–56.

The '786 patent discloses that

2 α ,3 β ,12 β -trihydroxydammar-20(22)-E,24-diene-3-O-[β -D-glucopyranosyl-(1 $\rightarrow$)- β -D-glucopyranoside] named “damulin A” and 2 α ,3 β ,12 β -trihydroxydammar-20,24-diene-3-O-[β -D-glucopyranosyl-(1 $\rightarrow$)- β -D-glucopyranoside] named “damulin B”, which are novel dammarane-based saponins and have a capability for enzymatic activation of AMP-activated protein kinase (AMPK), are separated and analyzed from a *Gynostemma pentaphyllum* extract by using HPLC and NMR. The damulin A and the damulin B have the following structures.

[Formula 1]



Id. at 3:3–48. The process of separating the damulins from a *Gynostemma pentaphyllum* extract and the preparation of the *Gynostemma pentaphyllum* extract include extracting from dried *Gynostemma pentaphyllum* leaves using an ethanol aqueous solution having a volume 10 to 20 times as large as the volume of the leaves, taking out a first supernatant, adding an ethanol aqueous solution (6 to 20 times), taking out a second supernatant through a 1 to 8 hour extraction at 65–95° C, putting the first and second supernatants together and filtrating to result in an extracted product, concentrating to provide a *Gynostemma pentaphyllum* extract concentrate (referred to as “TG1022”), and then treating the TG1022 with a high temperature and a high pressure to provide a *Gynostemma pentaphyllum* extract concentrate having increased contents of damulins (referred to as “TG1022F”). *Id.* at 3:49–4:3.

In its “EXAMPLE 1,” the ’786 patent discloses separation of damulin as an AMPK activating material from a *Gynostemma pentaphyllum* extract, in which “5 kg of dried *Gynostemma pentaphyllum* leaves was dipped in 50 l of 50% ethanol, and then, after [a] first extraction at 90° C. for 6 hours, a first supernatant was collected” and to “the residual ethanol-dipped material of the *Gynostemma pentaphyllum* leaves, 50 l of 50% ethanol was again added, and then a second supernatant was collected through 6 hour extraction at 90° C.” *Id.* at 7:35–46. In its “EXAMPLE 6,” the ’786 patent discloses preparation of *Gynostemma pentaphyllum* extract having increased damulin contents through treatment of high temperature and high pressure, in which the “*Gynostemma pentaphyllum* extract (TG1022F) was prepared by performing a high temperature/high pressure reaction or a ultra-high pressure reaction on the conventional *Gynostemma pentaphyllum* extract (TG1022) obtained by ethanol extraction at room temperature and

atmospheric pressure” and then in a high temperature/high pressure reaction, “a conventional high temperature/high pressure sterilizer (autoclave) or a ultra-high pressure reactor” is used. *Id.* at 12:15–45. Table 2 of the ’786 is reproduced below.

TABLE 2				
Reaction conditions			Content of damulins %	
temperature	Time	Pressure	(w/w)	
(° C.)	(Hour)	(atmosphere)	damulin A	damulin B
Control group (TG1022)			0.37 ± 0.03	0.28 ± 0.02
121	0.5	1.2	0.70 ± 0.04	0.56 ± 0.04
	1		0.89 ± 0.07	0.68 ± 0.04
	2		1.53 ± 0.06	1.16 ± 0.07
	3		2.01 ± 0.08	1.47 ± 0.08
	4		2.49 ± 0.09	1.81 ± 0.10
	8		3.21 ± 0.03	2.42 ± 0.03
	12		4.51 ± 0.03	4.12 ± 0.02
	24		6.82 ± 0.06	5.54 ± 0.05
45	12	297	0.62 ± 0.03	0.52 ± 0.02
		691	0.83 ± 0.07	0.74 ± 0.07
		1087	1.21 ± 0.06	1.13 ± 0.06
	24	297	0.82 ± 0.02	0.71 ± 0.05
		691	1.22 ± 0.04	0.97 ± 0.03
		1087	1.81 ± 0.06	1.33 ± 0.02

Id. at 13:1–20. Table 2 shows various conditions for producing *Gynostemma pentaphyllum* extracts which indicate an increase of damulin content in the *Gynostemma pentaphyllum* extract when high temperatures and high pressures are used. *Id.* at 12:65–67.

1. Illustrative Claims

Claims 1, 8, and 10 are the independent claims challenged by Petitioner in this proceeding. Independent claims 1, 8, and 10, reproduced below, are illustrative of the subject matter:

1. A method for preparing a novel *Gynostemma pentaphyllum*⁹ extract having increased concentrations of damulin A and damulin B, comprising the step of:

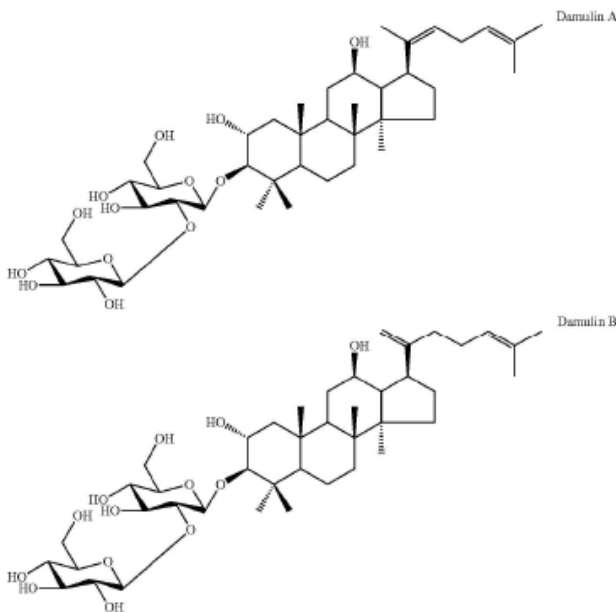
⁹ *Gynostemma pentaphyllum*, *G. pentaphyllum* and GP are used interchangeably throughout this decision.

subjecting an ethanol extract of *Gynostemma pentaphyllum* leaves to a temperature of about 40-125° C. and a pressure of about 1.2~1100 atmospheres for 1-24 hours to obtain increased concentrations of damulin A and damulin B, which are 0.7-7% (w/w) and 0.5-6% (w/w), respectively, based on the total weight of a dry powder of the novel *Gynostemma pentaphyllum* extract.

Ex. 1001, 16:60–17:2.

8. A pharmaceutical composition for improving and treating a metabolic syndrome, comprising at least one of at least 0.7% damulin A and at least 0.5% damulin B, represented by Formula 1:

[Formula 1]



and a pharmacologically acceptable carrier or excipient, wherein the metabolic syndrome is obesity, diabetes, or hyperlipidaemia.

Id. at 17:25–18:3.

10. A novel *Gynostemma pentaphyllum* extract comprising 0.7-7% (w/w) of damulin A and 0.5-6% (w/w) of damulin B based on the total weight of a dry powder of the *Gynostemma pentaphyllum* extract.

Id. at 18:7–10.

II. ANALYSIS

A. *Principles of Law*

“In an IPR, the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3) (requiring *inter partes* review petitions to identify “with particularity . . . the evidence that supports the grounds for the challenge to each claim”)). This burden of persuasion never shifts to Patent Owner. *See Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (discussing the burden of proof in *inter partes* review).

To prevail in its challenge to Patent Owner’s claims, Petitioner must demonstrate by a preponderance of the evidence¹⁰ that the claims are unpatentable. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time of the invention to a person having ordinary skill in the art. *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 “the scope and content of the prior art”; “differences between the prior art and the claims at issue”; and “the level of ordinary skill in the pertinent art.” *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

¹⁰ The burden of showing something by a preponderance of the evidence requires the trier of fact to believe that the existence of a fact is more probable than its nonexistence before the trier of fact may find in favor of the party who carries the burden. *Concrete Pipe & Prods. of Cal., Inc. v. Constr. Laborers Pension Tr. for S. Cal.*, 508 U.S. 602, 622 (1993).

In analyzing the obviousness of a combination of prior art elements, it can be important to identify a reason that would have prompted one of skill in the art “to combine . . . known elements in the fashion claimed by the patent at issue.” *KSR*, 550 U.S. at 418. A precise teaching directed to the specific subject matter of a challenged claim is not necessary to establish obviousness. *Id.* Rather, “any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.* at 420. Accordingly, a party that petitions the Board for a determination of unpatentability based on obviousness must show that “a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.” *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (citations omitted).

B. *Level of Ordinary Skill in the Art*

In determining the level of skill in the art, we consider the type of problems encountered in the art, the prior art solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Indus. Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986); *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1011 (Fed. Cir. 1983).

Petitioner asserts that a person of ordinary skill in the art would have had “an undergraduate science degree and would also have a Ph.D. in chemistry, pharmaceutical science, food science, or chemical engineering,

and several years of experience with extraction and analysis of pharmaceutically active materials from plant-based materials in an industrial or academic setting” and “would be familiar with the structure and utility of saponins, and generally aware of the scientific literature related to the extraction and pharmaceutical utility of gypenosides from GP and ginseng.” Pet. 13 (citing Ex. 1003 ¶ 18). Patent Owner does not dispute Petitioner’s definition of the person of ordinary skill. Prelim. Resp. 12. Because Petitioner’s proposed definition is unopposed and appears consistent with the Specification and art of record, we apply it here.

C. *Claim Construction*

In an *inter partes* review for a petition filed on or after November 13, 2018, “claim[s] of a patent . . . shall be construed using the same claim construction standard that would be used to construe the claim[s] in a civil action under 35 U.S.C. [§] 282(b), including construing the claim[s] in accordance with the ordinary and customary meaning of such claim[s] 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* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018) (codified at 37 C.F.R. § 42.100(b) (2019)) (amending 37 C.F.R. § 42.100(b) effective November 13, 2018). A term’s ordinary and customary meaning “is its meaning to the ordinary artisan after reading the entire patent.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1321 (Fed. Cir. 2005) (en banc). Nevertheless, “it is always necessary to review the specification to determine whether the inventor has used any terms in a manner inconsistent with their ordinary meaning,” because “[t]he specification acts as a dictionary when it

expressly defines terms used in the claims or when it defines terms by implication.” *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

Petitioner requests construction of the terms “an effective amount for improving or treating the metabolic syndrome” in claims 11–13 as meaning “an amount that produces any measurable amount of improvement in the metabolic syndrome” (Pet. 13–15 (citing Ex. 1003 ¶ 91)) and “[a] pharmaceutical composition for improving and treating a metabolic syndrome, comprising at least one of at least 0.7% damulin A and at least 0.5% damulin B . . . and a pharmacologically acceptable carrier or excipient” in claim 8 as meaning “a pharmaceutical composition that includes an extract with 0.7% and 0.5% of damulin A and damulin B[, respectively,] along with a carrier or excipient” (*id.* at 15–16 (citing Ex. 1002, 64–65, 251–52, 280; Ex. 1001, 12:15–67, Table 2)).

Patent Owner argues that “these constructions are not necessary.” Prelim. Resp. 13.

We determine that is not necessary for purposes of this Decision to construe any claim terms. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (only terms that are in controversy need to be construed, and only to the extent necessary to resolve the controversy)

D. *Overview of Asserted References*

1. *Kim 460 (Ex. 1005)*

Kim 460 “relates to a processed ginseng product with enhanced pharmacological effects and to a drink composition containing the processed ginseng product.” Ex. 1005, 1:7–10. Kim 460 explains that ginseng is known to have various pharmacological effects ranging from preventing

aging to providing anti-diabetic effects. *Id.* at 1:23–30. Kim 460 discloses enhancing these pharmacological effects by way of “a heat-treatment of a ginseng at a high temperature of 120° to 180° C. for 0.5 to 20 hours so as to make a ratio of ginsenoside (Rg₃+Rg₅) to (Rc+Rd+Rb₁+Rb₂) of above 1.0.” *Id.* at 1:10–16. Fresh ginseng is used, which can be Panax ginseng, and preferably, the treatment is at a temperature of 120° to 140° C. for 2 to 5 hours but the heating time can vary depending on the heating temperature. *Id.* at 3:13–25. To increase efficiency, the process may be performed in an airtight container such as an autoclave with the ginseng being soaked in water. *Id.* at 3:29–34. Alternatively, the processed ginseng may be extracted by using a solvent and then removing the solvent by concentrating or freeze-drying to obtain a dried power form. *Id.* at 3:41–47. The solvent can be water, a lower alcohol such as methanol or ethanol, a lower ketone, or a mixed solvent. *Id.* at 3:48–51. The processed ginseng product can be used as a variety of medicinal agents or can be incorporated as a food product. *Id.* at 4:34–44.

Kim 460’s Table 1 is reproduced below.

TABLE 1							
Relative Peak Area of Saponin Components of Ginseng							
Sample	Saponin						(Rg ₃ + Rg ₅) / (Rc + Rd + Rb ₁ + Rb ₂)
	Rb ₁	Rb ₂	Rc	Rd	Rg ₃	Rg ₅	
130° C./2 hrs	4.06	3.44	3.98	3.82	21.00	16.17	2.43
120° C./3 hrs	10.82	6.91	8.52	7.64	28.01	14.01	1.24
120° C./2 hrs	10.46	7.74	10.66	5.58	24.12	11.35	1.03
110° C./2 hrs	19.02	11.55	10.68	8.37	7.02	4.39	0.23
White Ginseng	22.15	3.25	5.86	2.47	0.00	0.00	0.00
Red Ginseng	30.11	9.69	12.45	1.76	1.05	1.05	0.01

Id. at 6:5–26. Table 1 shows heat treatments for various samples of ginseng producing amounts of ginseng saponin components of ginsenoside Rb₁, Rb₂, Rc, Rd, and Rg₃, and the ratios of (Rg₃+Rg₅)/(Rc+Rd+Rb₁+Rb₂) as shown.

Id. at 5:35–6:26.

Kim 460's Table 2 is reproduced below.

TABLE 2									
Change in Contents of Ginsenoside Rg ₃ and Rg ₅ Due to a Change in heating temperature									
Ginsenoside	Untreated Ginseng	Heating Temp. (°C.) Times (hrs)							
	(Fresh Ginseng)	100 (2)	110 (2)	120 (2)	130 (2)	150 (2)	160 (2)	180 (2)	200 (2)
Rg ₃	0.00	0.02	0.08	0.17	0.86	0.44	0.45	0.35	0.23
Rg ₅	0.00	0.02	0.05	0.08	0.44	0.53	0.56	0.48	0.38

Note) Contents of each components are expressed as % by weight based on the amount of a fresh ginseng.

Id. at 6:50–63. Table 2 shows the amounts of saponin components of ginsenoside Rb₃ and Rb₅ in ginseng samples that were heated at 100°, 110°, 120°, 130°, 150°, 160°, 180° and 200° C. for 2 hours in comparison to ginseng which was not heat-treated (“fresh ginseng”). *Id.* at 6:37–63.

2. Razmovski (Ex. 1007)

Razmovski is titled “Chemistry and pharmacology of *Gynostemma pentaphyllum*.” Ex. 1007, 197. Razmovski discloses that “[t]he dammarane saponins isolated from *Gynostemma pentaphyllum*, namely gypenosides or gynosaponins, are believed to be the active components responsible for its various biological activities and reported clinical effects” and that “*Gynostemma pentaphyllum* may complement the popular herbal medicine, *Panax ginseng*, as it also contains a high ginsenoside content and exhibits similar biological activities.” *Id.* (Abstr.). According to Razmovski, “*G. pentaphyllum* (usually dried material) can be extracted with a variety of

solvents, including water, methanol and ethanol for the more polar material; ethyl acetate, petroleum ether and chloroform for the less polar material, using an open system or under reflux.” *Id.* at 199. Over 100 saponins have been isolated and identified from *G. pentaphyllum*. *Id.* Of those, eight saponins are the same as protopanaxadiol-type ginsenosides Rb₁, Rc, Rb₃, Rd, F₂, Rg₃, malonyl-Rb₁, and malonyl-Rd that are found in *P. ginseng*, and together, these ginsenosides make up around 25% of the total gynosaponin in the plant. *Id.* at 200. “Total saponin content is reported to be about 2.4% of the dried herb.” *Id.* Razmovski provides Table 1 listing “Saponine structures [R1, R2, R3, R4, R5, R6, and R7] of the dammarane type in *G. pentaphyllum*.” *Id.* at 201–05.

Razmovski discloses a study shows that *G. pentaphyllum* has a “lipid lowering effect” in rats and quails. *Id.* at 200. Another study shows that in rats, *G. pentaphyllum* extract reduced serum triglyceride (TG) by 53% and by 85% in a 4 days treatment and in a 12 days treatment, respectively. *Id.* at 206–07. Clinical studies also show beneficial blood lipid change in hyperlipidaemic patients. *Id.* at 207–08. Other studies show that the saponin from *G. pentaphyllum* improves sensitivity to insulin receptors in diabetic rats. *Id.* at 208–09.

3. Kang (Ex. 1010)

Kang is titled “Composition Containing Ginsenoside Rg5 and Rk1 for improvement of Brain Function and Cognitive Function.” Ex. 1010, code (54). Kang explains that “[g]insenoside Rg3 (R), Rg3 (S), Rg5, and Rk1 are present in trace amounts in red ginseng and are known to have anti-epileptic effects.” *Id.* at 3. Kang discloses that ginsenoside Rg5 and Rk1 may be purified and separated from the roots of Panax plants containing ginseng

saponin, such as *Panax ginseng*, or *Gynostemma pentaphyllum* which contains “a compound of the dammaran[e] backbone, and the like, leaves of these plants, tissue cultures of these plants, or extracts thereof with water or lower alcohols.” *Id.* at 4.

Kang discloses a ginsenoside Rg5 and Rk1-containing pharmaceutical composition that “comprises 0.1 wt% to 50 wt% of the compounds based on the total weight of the composition” and discloses that the composition may further include “suitable carriers, excipients and diluents typically used in preparation of the pharmaceutical composition.” *Id.* at 4–5. In Kang’s “Example 1,” a composition containing ginsenoside Rg5 and Rk1 is prepared by obtaining a methanol extract through reflux extraction of ginseng in methanol via heating at 130°C for 2 hours. *Id.* at 7. This example produces 20 g of a fraction containing ginsenoside Rg5 and Rk1. *Id.* In Kang’s “Comparative Example 1,” ginsenoside Rg3 is prepared by “a typical method of separating an extract from ginseng with an alcohol extraction solvent” in which “20 g of ginseng crude-saponin was prepared and heated at 120°C for 3 hours.” *Id.* This example produces “2.01 g of ginsenoside (20S)-Rg3 and 1.7 g of ginsenoside (20R)-Rg3.” *Id.*

4. *Baek (Ex. 1008)*

Baek is titled “Dammarane Compound-Containing Pharmaceutical Composition for Renal Protection.” Ex. 1008, code (54). Baek’s pharmaceutical composition is used for a variety of ailments such as renal disease and diabetic nephropathy. *Id.* at Claims 1, 3. The composition includes a dammarane compound as an effective ingredient which can be ginsenoside Rk3 or ginsenoside Rh4. *Id.* ¶ 4. Baek explains that dammarane is a triterpenoid compound and is mainly found in *Panax* species in nature,

such as *Panax ginseng*, but “is also found in *Gynostemma pentaphyllum* Makino, which is not a *Panax* species.” *Id.* ¶ 6. Baek discloses that “[w]hen heated, dammarane generates Rg2, Rg3, Rh2, and Rh1 through release of glycosyl residues and then generates Rg5, Rk1, Rh3, F4, and Rh4 through dehydration at position 20.” *Id.* ¶ 9. Baek further explains that it is known the main ingredients of the ginseng extract include ginsenosides Rg3, Rg5, and Rk1, which exhibit renal protective activities. *Id.* ¶ 13. Baek purports to provide a pharmaceutical composition that includes dammarane compounds not present in nature and can be used for renal protection. *Id.* ¶ 15.

Baek discloses that from a *Panax* species or a *Gynostemma pentaphyllum* Makino,

dammarane is heated to 50°C to 200°C, specifically 120°C, for 30 minutes to 10 hours, specifically 3 hours, followed by one or more, specifically three, filtration stages using reflux extraction in a solvent selected from the group consisting of lower alcohols or mixtures thereof, specifically CH₃OH, and then the resulting filtrates are combined and concentrated under reduced pressure, thereby obtaining a CH₃OH extract, which, in turn, is dried under reduced pressure, suspended in water, and separated into a CH₂Cl₂ fraction, an n-BuOH fraction, and an H₂O fraction by sequentially using CH₂Cl₂ and water-saturated n-BuOH. Then, the fractions are dried by evaporation under reduced pressure, thereby obtaining CH₂Cl₂, n-BuOH, and H₂O extracts, respectively.

Id. ¶ 33. In another example, ginsenosides Rk3 and Rh4 are isolated by subjecting 1 kg of white ginseng to a heat treatment of 120°C for 3 hours, followed by three filtration stages using reflux extraction in CH₃OH for 3 hours. *Id.* ¶ 56.

5. *WO 178 (Ex. 1006)*

WO 178 “relates to a pharmaceutical composition and functional health food comprising an extract of processed *Panax* genus plant as an active ingredient for preventing and treating obesity and the use thereof.” Ex. 1006 ¶ 1. WO 178 explains that the plant belonging to the *Panax* genus has dammarane saponin as its most important ingredient and as an example, “Korean ginseng comprises high amount of ginsenosides, such as ginsenoside RbI, Rb2, Rc, Rd, RgI, Re and etc.” *Id.* ¶ 18. It is known to prepare a processed ginseng by high temperature and high pressure such that the main ginseng saponins, such as ginsenosides RbI, Rb2, Rc, and Rd, are changed into new saponin metabolites such as ginsenosides Rg3, Rg5, and RkI, that provide “new and more potent pharmacological effects.” *Id.* ¶ 19. One such *Panax* genus that has a root, stem, or leaf for this preparation is *Panax ginseng*. *Id.*

WO 178 purports to provide “a pharmaceutical composition comprising an extract of processed ginseng so as to make a ratio of ginsenoside (Rg3+Rg5+Rk1) to (Rb1+Rb2+Rc+Rd) of over 1.0, as an active ingredient in an effective amount to treat and prevent obesity.” *Id.* ¶ 26. The composition may comprise a filtrate with a residue that is concentrated “to obtain [an] extract, as [the] active ingredient and pharmaceutically acceptable carrier, diluents or adjuvants to treat and prevent obesity.” *Id.* ¶ 32.

To make its composition, WO 178 discloses a process that includes autoclaving a dried plant material from the *Panax* genus at a temperature ranging from 70 to 150°C, preferably 100 to 130°C, for a period ranging from 2 to 6 hours, preferably 3 to 5 hours; mixing the material with 1 to 20-fold, preferably, 3 to 10-fold weight (kg) of water, C₁–C₄ lower alcohol,

such as methanol, ethanol, butanol or the mixtures thereof, preferably ethanol; and then heating for the period ranging from 3 to 10 hours, preferably 3 to 6 hours, by reflux extraction with water, cold water extraction, ultra-sonication or conventional extraction. *Id.* ¶ 44.

6. *Huh (Ex. 1020)*

Huh is titled “Treatment of Insulin Resistance Syndrome” and was published on November 2, 2006. Ex. 1020, codes (43), (54). Huh “describes a composition that includes an extract of *Gynostemma pentaphyllum* used to treat insulin resistance syndrome, obesity, hypertriglyceridemia, as well as decrease body fat mass.” *Id.* at code (57). In its “Example 1” Huh discloses a process of preparing *Gynostemma pentaphyllum* (GP) including subjecting macerated GP leaves to an extraction process using aqueous alcohol (such as 70% ethanol); repeating this same step to recover a second aqueous alcohol extract eluate, and pooling the two extracts; evaporating the alcohol and further mixing the solution with distilled water and filtering; further mixing the solution with 1-BuOH, water layer, and evaporating off 1-BuOH; and recovering the organic material by reducing the liquid portion of pooled eluates by air drying and forming GP extract powder. *Id.* ¶¶ 80–86. Huh discloses that animals that were administered with its GP extract show an increased AMPK (AMP-activated protein kinase) activity, which is indicative of improved insulin resistance. *Id.* ¶ 120.

E. *Obviousness in view of Kim 460 and Razmovski*

Petitioner contends that claims 1–13 are rendered obvious under 35 U.S.C. § 103 over Kim 460 and Razmovski. *See* Pet. 22–41. Patent Owner opposes. Prelim. Resp. 17–40.

We address the parties' contentions with respect to the independent claims below.

1. Claim 10

Independent claim 10 recites “[a] novel *Gynostemma pentaphyllum* extract comprising 0.7-7% (w/w) of damulin A and 0.5-6% (w/w) of damulin B based on the total weight of a dry powder of the *Gynostemma pentaphyllum* extract.” Ex. 1001, 18:7–10.

Petitioner contends that “Kim 460 discloses that a ‘conventional use’ of its [ginseng] extractions is a medicinal agent.” Pet. 35 (citing Ex. 1005, 4:40–41). Kim 460 “states that an extract [of ginseng] with increased levels of Rg3 and Rg5 is useful for treating diabetes.” *Id.* (citing Ex. 1005, 9:8–25). “Kim 460 teaches extracting saponins from ginseng using ethanol as a solvent Kim 460 heats ginseng or an extract of ginseng at 120°–180° C. for 0.5 to 20 hours.” Pet. 23 (citing Ex. 1005, 3:13–23, 3:48–49, 4:21–22).

Razmovski, relied on by Petitioner, “shows that ginsenosides Rb1, Rb2, Rc and Rd are present in [*Gynostemma pentaphyllum* (GP)], and observes that ginsenosides make up 25% of the saponin content of GP.” Pet. 24 (citing Ex. 1007, 200 (Table 1)). According to Petitioner, “Razmovski teaches that GP contains a significant and useful amount of the same ginsenosides that are used by Kim 460.” *Id.* “Razmovski teaches that saponins in GP have ‘biological activities congruent to the very popular expensive herbal medicine, *P. ginseng*.’” *Id.* (citing Ex. 1007, 214).

Based on these teachings in Kim 460 and Razmovski, Petitioner concludes that a person of ordinary skill in the art would have been

motivated to substitute GP for the ginseng (as taught by Razmovski) in the process of Kim 460: heating a GP extract to 120-180 °C in an autoclave for 0.5 to 20 hours to transform the

Rb1, Rb2, Rc and Rd in the GP extract (as taught by Razmovski) to Rg3 and Rg5 and Rk1.

Pet. 24 (citing Ex. 1003 ¶ 102). Especially since the same source material Rb1, Rb2, Rc and Rd is shown by Razmovski to be present in GP. *Id.* (citing Ex. 1003 ¶¶ 35, 102).

Patent Owner contends that the Experimental Reports provided by Petitioner are not evidence of inherency, that the test results in the Experimental Reports are unreliable, and that Wu does not replicate the experiments of Kim 460. *See* Prelim. Resp. 20.

a) Experimental reports

Patent Owner contends that “Petitioner did not adhere to methods disclosed in the prior art to obtain the experimental results.” Prelim. Resp. 20, 23. Specifically, Patent Owner contends that the heating conditions used in the Petitioner’s experimental set uses “130°C for 3 hours, which is neither disclosed in Examples of Kim 460 nor within the temperature range of claim 1.” *Id.* at 25.

Kim 460 teaches heat treating ginseng “at a temperature of 120° to 180° C. for 0.5 to 20 hours, *preferably at a temperature of 120° to 140° C. for 2 to 5 hours*. The heating time varies depending on the heating temperature.” Ex. 1005, 3:21–24 (emphasis added). Kim 460 teaches that “the heating process may be preferably performed in an airtight container such as [an] autoclave.” *Id.* at 3:30–33. Either a small amount of water is added to the ginseng or the ginseng is soaked in water and then heated in a closed container. *Id.* at 3:33–35. Kim 460 teaches that heat treating at 120 to 180° C significantly increases the Rg3 and Rg5 content compared to fresh ginseng. Ex. 1005, 6:65–7:3; *see also id.* at 6:49–64 (Table 2, showing highest Rg3 and Rg5 content at 130°C treatment for 2 hours). Kim 460

teaches that the ginseng is then dried or further processed. *See id.* at 3:35–40.

Kim 460 teaches that the heat processed ginseng can be further processed using a solvent. “Specifically, the processed ginseng is extracted by using a solvent, and then the solvent is removed by concentrating or freeze-drying to obtain a processed ginseng extract as dried powders.” *Id.* at 3:43–46. The solvent which may be employed by Kim 460 includes water, methanol, ethanol, acetone, methylethylketone or mixtures thereof. *Id.* at 3:47–51.

Kim 460 shows that heat treating ginseng changes the “saponin components Rg₃ and Rg₅ which are absent or present in a trace amount in a commercial white ginseng or red ginseng, so they exhibit superior pharmacological effects.” *Id.* at 6:31–34, 6:5–25 (Table 1). Kim 460 teaches that “the processed ginseng having a ratio of ginsenoside (Rg₃+Rg₅) to (Rc+Rd+Rb₁+Rb₂) of above 1.0 . . . was stronger [by] about 50 fold than that of the original white ginseng extract which was not heat-treated at 50% vasodilation concentration.” *Id.* at 9:13–18. In other words, Kim 460 teaches that heat-treating ginseng material that contains Rc+Rd+Rb₁+Rb₂ transforms the source material to contain increased amounts of ginsenoside Rg₃+Rg₅ and results in a product that is more potent.

Based on these teachings in Kim 460, we agree with Petitioner that it would be reasonable to expect that the same source material derived from a different plant would behave similarly to heat treatment. *See* Pet. 24. Razmovski teaches that GP is suitable source of ginsenosides. *See* Ex. 1007, 199–200 (“These ginsenosides [identified from *G. pentaphyllum*] make up around 25% of the total gynosaponin in the plant and is the first example of ginseng saponins found outside of the Araliaceae family.”).

Razmovski teaches that ginsenosides Rb₁, Rc, Rb₃, Rg₃, malonyl-Rb₁ and malonyl-Rd are found in GP and are the same as those in *P. ginseng*. *Id.* at 200. The record, therefore, supports Petitioner's position that substituting GP for the ginseng starting material in Kim 460 as suggested by Razmovski would similarly increase the amount of ginsenoside Rg₃ + Rg₅ in an extract made from the GP starting material. *See also* Ex. 1005, 4:26–31 (“[T]he processed ginseng product according to the present invention wherein a ratio of ginsenoside (Rg₃+Rg₅) to (Rc+Rd+Rb₁+Rb₂) is above 1.0 shows superior physiological activities as different from the prior processed ginseng product in which ginsenoside components such as Rg₃ and Rg₅ are hardly present.”).

Our reviewing court has “recognized that inherency may supply a missing claim limitation in an obviousness analysis.” *PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014). “[O]ur early precedent, and that of our predecessor court, established that the concept of inherency must be limited when applied to obviousness, and is present only when the limitation at issue is the ‘natural result’ of the combination of prior art elements.” *Id.* at 1195.

Inherency may supply a missing claim limitation in an obviousness analysis. An inherent characteristic of a formulation can be part of the prior art in an obviousness analysis even if the inherent characteristic was unrecognized or unappreciated by a skilled artisan. It is long settled that in the context of obviousness, the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not distinguish a claim drawn to those things from the prior art. The Supreme Court explained long ago that it is not invention to

perceive that the product which others had discovered had qualities they failed to detect.

Persion Pharms. LLC v. Alvogen Malta Operations Ltd., 945 F.3d 1184, 1189 (Fed. Cir. 2019) (citations, internal quotations marks, brackets and parentheticals omitted).

The Experimental Report-1 provided by Petitioner may not have used the methods exemplified in Kim 460, but the Experimental Report-1 made products using methods that apply a protocol within the *preferred* temperature range and treatment time as disclosed in Kim 460. *Compare* Ex. 1013¹¹, 112–13, *with* Ex. 1005, 3:24–25, 3:30–34. Petitioner’s Declarant, Dr. Davies, selected a treatment protocol that falls within the preferred treatment temperature and time disclosed in Kim 460. *See* Ex. 1003 ¶ 104; Ex. 1005, 3:21–24 (Kim 460 teaches heat treating ginseng “at a temperature of 120° to 180° C. for 0.5 to 20 hours, preferably at a temperature of 120° to 140° C. for 2 to 5 hours. The heating time varies depending on the heating temperature.”); Ex. 1013.

Briefly, the Experimental Report-1 discloses four different treatment methods. Three of the methods used in Experimental Report-1 applied heat and pressure for the extraction step, followed by reflux extraction with a solvent, and finally used freeze drying to obtain a powder from the extracts. *See* Ex. 1013. All three experiments tested two different GP samples. The initial treatment in all three methods of the Experimental Report-1 applied water to the plant material and applied a temperature of 130°C for 3 hours in an autoclave achieving a pressure of 1.56. mPa. *See* Ex. 1013, 10, 12. The second extraction step was a reflux extraction with a solvent using either

¹¹ We refer to Exhibit 1013 as the “Experimental Report-1.”

(1) water at 90°C for 4 hours; (2) 50% ethanol at 70°C for 4 hours; and (3) 50% methanol at 60°C for 4 hours. *See id.* at 10, 12, *see also id.* at 27 (“Gypenoside L, Gypenoside LI, Ginsenoside Rg3, Damulin A and Damulin B were all determined using the first three extraction methodologies of water and heat followed by reflux extraction in water, ethanol or methanol. The use of ethanol or methanol in the reflux extraction provides higher contents of all compounds analyzed compared to use of water alone.”).

Here, Petitioner has articulated a sufficient motivation for substituting GP for ginseng in Kim 460. *See* Pet. 1, 8, 24; Ex. 1003 ¶¶ 33, 69, 78, 83, 102; Ex. 1007, 199. There is a reasonable expectation that the ginsenosides present in GP as taught by Razmovski would similarly transform into the desired Rg₃+Rg₅ substituents that Kim 460 teaches have the increased activity after following the treatment protocols in Kim 460. The Experimental Report-1 shows that the damulin A and damulin B concentration are within the range recited in claim 10. *See* Ex. 1013, 26–27. “The use of ethanol or methanol in the reflux extraction provides higher contents of all compounds analyzed compared to use of water alone.” *Id.* at 27. We note that the water extraction of plant sample GP-WW-02 sample provided a damulin B concentration just below the level recited in claim 10. However, this result could be batch specific because the damulin level was lower for this plant sample in all extraction protocols when compared to the plant sample GP-WW-01. *See id.* at 26.

b) Unreliable results

Patent Owner contends that Petitioner’s use of highly impure damulin B standard makes the results unreliable. Prelim. Resp. 26. Patent Owner further contends that Petitioner never explained why Petitioner’s

Declarant found the damulin B standard too impure for use in Exhibit 1016 but sufficient to measure the concentrations in Exhibit 1013. Prelim.

Resp. 27.

We are not persuaded by Patent Owner's argument. Dr. Lee does not indicate what standard they used in the Experimental Report-2. *See* Ex. 1016.¹² Thus, there is no indication whether the damulin B standard used in Exhibits 1016 and 1013 was the same standard from the same lot. All that we know is that "[t]he content of damulin B [in Experimental Report -2] was not determined, because the purity of the standard used for damulin B was too low to determine the content, and a chromatography of damulin B sample showed a double peak." Ex. 1016, 2; Ex. 1017 ¶¶ 18–19.

Experimental Report-1 indicates that the "Damulin B(DB) was purchased from Chengdu Biopurify Phytochemicals Ltd. China, purity of 74%. Its isolation and purification were too difficult to purchase higher purity of standard." Ex. 1013, 5. The mass spec analysis in Experimental Report-1 does not show a double peak at m/z 781.1. *See* Ex. 1013, 23. Because there is no indication on this record that the same standard was used in the different experiments leading to the different Experimental Reports, we are not persuaded by Patent Owner's contention that the results are necessarily unreliable because the standard used for measuring the content of damulin B was less than ideal.

c) Pressure

Patent Owner contends that Petitioner fails to establish that the claimed pressure is necessarily present in the combination of Kim 460 and Razmovski. Prelim. Resp. 30. According to Patent Owner, "Petitioner's

¹² We refer to Exhibit 1016 as "Experimental Report-2."

Expert speculates without support that “[h]eating in an autoclave elevates pressure, and heating to the temperatures of 120° to 180° C described by Kim 460 would increase the pressure to more than 1.2 atmospheres.” *Id.* at 31 (citing Ex. 1003 ¶ 41) (alteration in original). Patent Owner contends that “Petitioner fails to establish motivation to apply high temperature and high pressure to ethanol extracts of GP leaves.” *Id.* at 34.

We are not persuaded by Patent Owner’s contention that Petitioner has failed to establish that heating a sample in a closed vessel will increase the pressure inside the vessel. Dr. Davies’ testimony relies on the ideal gas law $PV=nRT$ to support the position that heating in an autoclave will increase the pressure inside the vessel. Based on the ideal gas law, Petitioner’s Declarant calculates that “pressure in an autoclave at 130° C was reported as 1.58 MPa.” Ex. 1003 ¶ 41 (citing Ex. 1013, 12); Pet. 23.

d) Post filing date reference

Patent Owner contends “Wu did not replicate Kim 460’s methods and fails to establish inherency based on disclosures or alleged suggestions of the prior art—Wu did not apply pressure and is not relevant to the inherency analysis of Kim 460.” Prelim. Resp. 22.

Extrinsic evidence can be used to demonstrate what is “necessarily present” in a prior art embodiment even if the extrinsic evidence is not itself prior art. *See Monsanto Tech. LLC v. E.I. DuPont de Nemours & Co.*, 878 F.3d 1336, 1345 (Fed. Cir. 2018) (allowing “non-prior art data” to be used to support inherency); *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (finding that the prior art need not recognize the inherent property).

Wu discloses that “[t]he leaves of crude and heat-processed *G. pentaphyllum* (5.0 g) were extracted with 50 mL of 80% methanol by ultrasonication for 1.5 h and then evaporated.” Ex. 1012, 311. Wu shows that extracts from “*G. pentaphyllum* heat processed at 130 °C for 3 h [results in damulin A content of 11902 µg/g, damulin B content of 5877 µg/g], whereas those from the raw plant were below 250 µg/g. Longer treatment times (>3 h) did not give any significant changes in the saponin contents.” *Id.* at 315. Wu, however, does not disclose how the samples are heat processed. Because it cannot be established based on Wu’s disclosure that the samples are autoclaved, just like the samples in Kim 460, we agree with Patent Owner that Wu cannot be relied on to establish inherency of Kim 460’s process when applied to *G. pentaphyllum*.

a) Reliance on the ’786 specification

Patent Owner contends that “Petitioner cannot show inherency by relying on results in Table 2 of the ’786 patent because Petitioner’s references fail to disclose or suggest methods used to obtain those results.” Prelim. Resp. 20, 28.

In this Decision we do not rely on the teachings in Table 2 of the ’786 patent; therefore, we do not need to address whether Petitioner’s reliance on this information in the Petition is appropriate.

b) Claim 10 summary

Petitioner has sufficiently demonstrated that there is motivation to substitute GP for ginseng in Kim 460, and that applying a treatment protocol within Kim 460’s preferred range as shown by the Experimental Report-1 results in a product that contains damulin A and B at the requisite levels. Based upon our review of the current record, and consideration of the

parties' arguments and evidence, there is a reasonable likelihood that claim 10 of the challenged '786 patent is unpatentable and rendered obvious over Kim 460 and Razmovski.

2. *Claim 8*

Independent claim 8 recites “[a] pharmaceutical composition for improving and treating a metabolic syndrome, comprising at least one of at least 0.7% damulin A and at least 0.5% damulin B, represented by Formula 1: [(not shown)] and a pharmacologically acceptable carrier or excipient, wherein the metabolic syndrome is obesity, diabetes, or hyperlipidaemia.” Ex. 1001, 17:25–18:3.

Petitioner contends that Kim 460 teaches that an extract with “increased levels of Rg3 and Rg5 is useful for treating diabetes.” Pet. 35 (citing Ex. 1005, 9:8–25). Kim 460 suggests “that ginseng is commonly used for treating hyperlipidemia and diabetes, which are metabolic syndromes.” *Id.* (citing Ex. 1005, 1:25–30).

“Razmovski [similarly] discusses numerous studies finding that GP is effective for modulating lipid metabolism and hyperglycaemia.” Pet. 35 (citing Ex. 1007, 200, 206–209). Razmovski teaches that “[t]he major interest of *G. pentaphyllum* originated from its lipid lowering effects observed in animal models and human studies.” Ex. 1007, 214.

Petitioner contends that “it is obvious to substitute GP for ginseng, as taught by Razmovski, in the process of Kim 460, and that substitution would result in an extract with at least 0.7% of damulin A and 0.5% of damulin B” and apply the extract as a medicament for the purpose of treating metabolic disease. Pet. 36.

Patent Owner does not provide a separate argument for claim 8 relying instead on those arguments made for claim 1 and 10. Prelim. Resp. 15; *see id.* at 15 n.1).

Based upon our review of the current record, and consideration of the parties' arguments and evidence, there is a reasonable likelihood that claim 8 of the challenged '786 patent is unpatentable and rendered obvious over Kim 460 and Razmovski for similar reasons as for claim 10.

3. *Claim 1*

Independent claim 1 recites in pertinent part:

subjecting an ethanol extract of *Gynostemma pentaphyllum* leaves to a temperature of about 40-125° C. and a pressure of about 1.2~1100 atmospheres for 1-24 hours to obtain increased concentrations of damulin A and damulin B, which are 0.7-7% (w/w) and 0.5-6% (w/w), respectively, based on the total weight of a dry powder of the novel *Gynostemma pentaphyllum* extract.

Ex. 1001, 16:60–17:2 (emphasis added).

Petitioner relies on Razmovski for teaching that GP is a known equivalent for ginseng containing many of the same components. *See* Pet. 24 (citing Ex. 1003 ¶¶ 35 (“interchanging GP as a source of ginsenosides of Rb1, Rb2, Rc, and Rd which are chemically and pharmacologically identical to the ginsenosides in Kim 460”), 102). We agree with Petitioner that Razmovski reasonably supports the position that it would have been obvious to substitute GP for ginseng in Kim 460's methods. The question that remains, is whether there is a reason to subject an ethanol extract of GP to an elevated temperature and pressure.

Petitioner contends that Kim 460 teaches extracting saponins from ginseng using ethanol. Pet. 23 (citing Ex. 1005, 3:48–49). The text from Kim 460 relied on by Petitioner is reproduced below:

The solvent which may be employed herein includes a water, lower alcohol such as methanol, ethanol, etc., lower ketone such as acetone, methylethylketone, etc., supercritical fluid or mixed solvent thereof.

Ex. 1005, 3:48–51 (emphasis added).

Petitioner relies on this teaching in Kim 460's that methanol and ethanol are interchangeable. Example 3 of Kim 460 teaches subjecting an alcohol extract to heating in an autoclave at 120°C for 4 hours.

1 kg of dried fine root of ginseng was extracted with 2 liters of methanol under reflux in a water bath for 4 hours and then filtered to obtain a ginseng extract. The ginseng extract thus obtained was then dried under a reduced pressure. The ginseng extract obtained as syrup was placed into an autoclave and then was heated at 120° C. for 4 hours. The heat-treated ginseng extract was dried at 60° C. to obtain a processed ginseng extract as concentrated syrup.

Ex. 1005, 5:16–24.

According to Petitioner, “[h]eating in an autoclave elevates pressure, and heating to the temperatures of 120° to 180°C would increase the pressure to more than 1.2 atmospheres.” Pet. 23 (citing Ex. 1003 ¶ 41). Petitioner concludes that “performing the process of Kim 460, using an extract of GP (as taught by Razmovski), must result in the same extract. Performing the same heating process, on the same product, produces the same results.” Pet. 26.

Patent Owner contends that Petitioner fails to establish motivation to apply high temperature and high pressure to ethanol extracts of GP leaves. Prelim. Resp. 34 (citing *Polaris Indus., Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1070 (Fed. Cir. 2018) (holding it improper for the Office to “focus[] on what a skilled artisan would have been able to do, rather than what a skilled artisan would have been motivated to do at the time of the

invention’’)). Specifically, Patent Owner contends that “Kim 460 fails to disclose subjecting an ethanol extract to high pressure and high temperature.” Prelim. Resp. 28. Arguing that it is impermissible to use “a mixture of methods and deviated from the prior art’s examples using hindsight knowledge of the patent at issue.” *Id.* at 29.

Petitioner has sufficiently shown that there is a reason and motivation to substitute GP for ginseng in Kim 460. Razmovski teaches that “the saponin content of the [GP] plant has become the centre of extensive investigation which includes a variety of biological activities congruent to the very popular expensive herbal medicine, *P. ginseng*. Both contain dammarane-type glycosides, some of which are common to both plant species.” Ex. 1007, 214. Razmovski, therefore, teaches that GP is a more cost-effective source material for ginsenosides. *Id.*; *see also* Ex. 1022, 2 (“*G. pentaphyllum* could provide a variety of saponin types, an inexpensive source of saponins for pharmaceutical use and possibly, a substitute for *P. ginseng*”). Not only is GP an art recognized equivalent for ginseng, Razmovski also suggests that the lower cost associated with GP would further motivate the substitution.

Petitioner relies on Razmovski for teaching that GP is suitable source of ginsenosides. *See* Pet. 1, 8, 24; Ex. 1003 ¶¶ 33, 69, 78, 83, 102; Ex. 1007, 200 (“These ginsenosides [identified from *G. pentaphyllum*] make up around 25% of the total gynosaponin in the plant and is the first example of ginseng saponins found outside of the Araliaceae family”). Based on these teachings, Petitioner has sufficiently shown that substituting GP for the ginseng starting material in Kim 460 is reasonable. The ginsenosides present in GP as taught by Razmovski would similarly transform into the desired Rg₃+Rg₅ substituents that Kim 460 teaches has the increased activity.

Here, Kim 460 teaches an alcohol extraction method using methanol, following the extraction Kim 460 teaches applying placing the sample in an autoclave that was then heated 120°C for 4 hours. *See* Ex. 1005, 5:22.

Petitioner's Declarant, Dr. Davies, explains that heating in a closed container follows the ideal gas law and would raise the pressure inside the container. *See* Ex. 1003 ¶ 41. Kim 460, therefore, expressly teaches making an alcohol extract followed by heating the sample at the increased temperature and pressure. The alcohol used in Kim 460's method was methanol, however, Kim 460 suggests that other solvents can be used such as ethanol. *See* Ex. 1005, 3:48–51.

Based on our review of the record, at this stage of the proceeding Petitioner has sufficiently shown that Kim 460 suggests making an alcohol extract from ginseng followed by heat treating the extract. The teachings of Razmovski provide a reasonable expectation that substituting GP for ginseng in Kim 460's process would similarly transform the ginsenosides found in GP. *See* Pet. 24 (“[R]easonable expectation of success for this substitution since Razmovski shows that the source materials in Kim 460 (Rb1, Rb2, Rc and Rd) are all present in GP.”).

4. *Summary*

Based upon our review of the current record, and consideration of the parties' arguments and evidence, Petitioner has demonstrated sufficiently that, there is a reasonable likelihood that claims 1–13 of the challenged claims of the '786 patent are unpatentable and rendered obvious over Kim 460 and Razmovski.

Our determination in this Decision is not a final determination on the patentability of the challenged claims and, thus, leaves undecided any

factual issues necessary to determine whether sufficient evidence supports Petitioner’s contentions by a preponderance of the evidence in the final written decision. *See TriVascular, Inc. v. Samuels*, 812 F.3d 1056, 1068 (Fed. Cir. 2016) (noting in the context of an *inter partes* review that “there is a significant difference between a petitioner’s burden to establish a ‘reasonable likelihood of success’ at institution, and actually proving invalidity by a preponderance of the evidence at trial”) (quoting 35 U.S.C. § 314(a) and comparing § 316(e)).

F. *Obviousness in view of Kim 460 and Kang or Baek*

Petitioner contends that claims 1–13 are rendered obvious under 35 U.S.C. § 103 over Kim 460 and Baek or Kang. *See* Pet. 41–47. Patent Owner opposes. Prelim. Resp. 40–48.

Petitioner contends that Kim 460 describes overlapping process conditions for making extracts of ginseng. Pet. 41–42 (citing Ex. 1005, 3:13–35; Ex. 1003 ¶ 41).

According to Petitioner, “Kang is directed to a pharmaceutical composition with Rg5 and Rk1 as active ingredients. (Ex. 1010, claim 1). Kang creates Rg5 and Rk1 by heating an alcohol extract at 130 °C for 2 hours. (*Id.* at 7). Kang explicitly teaches using GP as an alternative to ginseng to create Rg5 and Rk1. (*Id.* at 4).” Pet. 42.

Kang recites:

Ginsenoside Rg5 and Rk1, . . . may be purified and separated through column chromatography by processing the roots of *Panax* plants containing ginseng saponin, for example, *Panax ginseng* . . . or *Gynostemma pentaphyllum* containing a compound of the dammaran[e] backbone, and the like, leaves of

these plants, tissue cultures of these plants, or extracts thereof with water or lower alcohols.

Ex. 1010, 4.

Petitioner relies on Baek for teaching “heating GP at a temperature of 50° to 200° C for 0.5 to 20 hours and extracting saponins from the heated GP using alcohol as a solvent.” Pet. 42 (citing Ex. 1008 ¶ 33). “Baek also discloses that GP is a substitute for ginseng as a source of dammarane saponins.” Pet. 43 (citing Ex. 1008 ¶¶ 6, 33). Petitioner concludes that it would have been obvious to one of ordinary skill in the art to substitute GP for ginseng in Kim based on the teachings of Kang and Baek. Pet. 43.

“Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious.” *In re Fout*, 675 F.2d 297, 301 (CCPA 1982); *see also In re Mayne*, 104 F.3d 1339, 1340 (Fed. Cir. 1997) (“Because the applicants merely substituted one element known in the art for a known equivalent, this court affirms [the rejection for obviousness].”). Because the teachings of Kang or Baek reasonably suggest that GP and ginseng are interchangeable (*see* Ex. 1010, 4; Ex. 1008 ¶ 28), we agree with Petitioner that on this record, at this stage of the proceeding, applying Kim 460’s extraction protocol to GP would render the claimed composition obvious for the reasons provided in the Petition. *See* Pet. 41–43, 47.

Petitioner relies on the Experimental Report-1 to establish that applying the heat treatment method of Kim 460 results in the recited damulin content. Experimental Report-1 shows experiments performed under the direction of Petitioner’s Declarant, Dr. Davies, to establish “that heating [GP] at 130 °C for 3 hours produces an extract with damulin levels that exceed the amounts of claim 8 [and fall with the range of claim 10]

using several different solvents.” Pet. 43 (citing Ex. 1013 (Tables 2–3); Ex. 1012, 315 (Table 2)).

Patent Owner presents similar arguments to those discussed above with respect to the combination of Kim 460 and Razmovski. *See* Prelim. Resp. 40–48.

For the same reasons discussed above (§ II.E), we are not persuaded by Patent Owner’s contention, and agree with Petitioner that either Kang or Baek reasonably suggest that GP is a suitable equivalent to ginseng for obtaining a pharmaceutical composition with Rg5 and Rk1 as active ingredients. *See* Ex. 1010, 4; Ex. 1008 ¶ 28

Based upon our review of the current record, and consideration of the parties’ arguments and evidence, Petitioner has demonstrated sufficiently that, there is a reasonable likelihood that claims 1–13 of the challenged claims of the ’786 patent are unpatentable and rendered obvious over Kim 460 and Kang or Baek.

G. *Obviousness in view of WO 178 and Razmovski*

Petitioner contends that claims 8–10, 12, and 13 are rendered obvious under 35 U.S.C. § 103 over WO 178 and Razmovski. *See* Pet. 47–55. Patent Owner opposes. Prelim. Resp. 48–53.

Petitioner contends that WO 178 “discloses heating ginseng at 70 to 150°C in an autoclave for 2 to 6 hours to convert dammarane saponins Rb1, Rb2, Rc and Rd into Rg3, Rg5 and Rk1, and extracting the converted saponins from the ginseng using an alcohol solvent.” Pet. 48 (citing Ex. 1006 ¶¶ 19, 26, 44). WO 178 performs heating in an autoclave, which would result in increased pressure. Pet. 49 (citing Ex. 1006 ¶ 44; Ex. 1003

¶ 41 (“The fact that heating a sealed vessel increases pressure is captured in the ideal gas law ($PV=nRT$).”).

Petitioner relies on Razmovski for teaching that GP includes several of the same saponins as ginseng, therefore, rendering obvious the substitution of GP for ginseng. *See* Pet. 48–49 (citing Ex. 1004 ¶ 36). Petitioner relies on the teachings of Razmovski to establish “that GP includes several of the same saponins as ginseng including Rb1, Rb2, Rc and Rd, and make up 25% of the saponin content of GP.” Pet. 48 (citing Ex. 1007, 200 (Table 1)). Petitioner contends that “an extract of GP that has been heated within the parameters described by WO 178, would have at least one of 0.7% of damulin A or 0.5% of damulin B.” Pet. 49.

Based on these combined teachings, Petitioner concludes that a person of ordinary skill in the art “would have a reasonable expectation of success for this substitution [of GP for ginseng in WO 178’s process] since Razmovski shows that the source materials in WO 178, Rb1, Rb2, Rc and Rd, are all present in GP.” Pet. 49 (citing Ex. 1003 ¶ 36).

Patent Owner argues that Petitioner has not provided a sufficient basis from which to conclude that the claimed composition and extract based on the combination of WO 178 and Razmovski are inherently obvious. *See* Prelim. Resp. 48–53.

WO 178 teaches producing an extraction of ginseng.

[D]ried plant material of *Panax* genus was cut into small pieces and the piece was autoclaved at the temperature ranging from 70 to 150°C, *preferably 100 to 130°C, for the period ranging from 2 to 6 hours, preferably 3 to 5 hours*; and was mixed with 1 to 20-fold, preferably, 3 to 10-fold weight (kg) of water, C₁-C₄ lower alcohol, such as methanol, ethanol, butanol or the mixtures thereof, *preferably ethanol*; was heated for the period ranging from 3 to 10 hours, preferably 3 to 6 hours, by reflux extraction

with water, cold water extraction, ultra-sonication or conventional extraction, preferably by reflux extraction with water; the residue was filtered and then the filtrate was dried at the temperature ranging from 40 to 80°C, preferably from 50 to 70°C, to obtain inventive extract of processed ginseng.

Ex. 1006 ¶ 44 (emphases added); *see also id.* ¶ 118 (“1 kg of dried root of *Panax ginseng* was cut into small pieces and the sliced pieces were heated at 120°C for 4 hours in autoclave. The processed ginseng was mixed with 2 I [sic] of ethanol and heated for 4 hours by reflux extraction with water.”). Ginseng processed at 120°C for 4 hours in an autoclave shows increased Rg3, Rg5, Rg1 content and a reduction of Rb1, Rb2, Rc, and Rd. *Id.* ¶ 127 (Table 1).

Petitioner’s Declarant, Dr. Davies, selected a treatment protocol for Experimental Report-1 that falls within the preferred treatment temperature and time disclosed in WO 178. *See* Ex. 1003 ¶¶ 104 (Explaining that “the experimental conditions of temperature, pressure and extraction solvent are within the processing conditions described by Kim 460, WO 178, and Baek.”), 105–107; Ex. 1006 ¶ 44; Ex. 1013. Experimental Report-1 shows that damulin A and B are within the claimed concentrations. *See* Ex. 1013, 26; Ex. 1003 ¶ 105 (“As expected, the use of methanol or ethanol with reflux extraction provided higher contents of all compounds analyzed compared to use of a simple water extraction alone The results are what I expected based on the prior art.”). According to Dr. Davies, results showing higher compound content in the examples that use methanol and ethanol extraction is expected. Ex. 1003 ¶ 105.

Based upon our review of the current record, and consideration of the parties’ arguments and evidence, Petitioner has demonstrated sufficiently that, there is a reasonable likelihood that claims 8–10, 12, and 13 of the

challenged claims of the '786 patent are unpatentable and rendered obvious over WO 178 and Razmovski.

H. *Obviousness in view of WO 178 and Kang*

Petitioner contends that claims 1–13 are rendered obvious under 35 U.S.C. § 103 over WO 178 and Kang. *See* Pet. 55–63.

Patent Owner opposes. Prelim. Resp. 48–53. Specifically, Patent Owner contends that “Kang’s disclosure informs a [person of ordinary skill in the art] about different methods for extracting ginsenosides from ginseng, but does not provide sufficient guidance to arrive at the claimed method for subjecting an ethanol extract of GP leaves to high pressure and high temperature as claimed to obtain the Claimed Concentrations.” *Id.* at 55.

With respect to claim 1, we agree with Patent Owner that Petitioner has not sufficiently explained why based on the teachings of Kang one would have substituted methanol for ethanol in Kang’s extraction method.

Based on that apparent deficiency, with respect to Kang’s extraction method, Petitioner has not made a sufficient showing that the Petition demonstrates that there is a reasonable likelihood that claims 1–13 are unpatentable over WO 178 and Kang.

I. *Obviousness in view of Huh*

Petitioner contends that Huh in combination with the knowledge of the person of ordinary skill in the art renders claims 8, 9, and 12 obvious. Pet. 64–67.

Patent Owner contends that Huh does not disclose or suggest damulin A or B of the claimed concentrations. Prelim. Resp. 58. Specifically, Patent Owner contends that Petitioner has not shown that damulin A or damulin B

is present in Huh's composition at the claimed ranges. *See generally id.* at 58–65.

Huh teaches making extracts from *Gynostemma pentaphyllum* for use with particular types of anti-hyperglycemic activity using the following steps:

- (a) extracting macerated *G. pentaphyllum* leaves in aqueous alcohol (such as 70% ethanol);
- (b) repeating step (a), recovering a second aqueous alcohol extract eluate, and pooling the two extracts;
- (c) evaporating the alcohol and further mixing the solution with distilled water and filtering;
- (d) further mixing the solution with 1-BuOH, water layer, and evaporating off 1-BuOH;
- (e) recovering the organic material by reducing the liquid portion of pooled eluates by drying (e.g., air drying), and forming *G. pentaphyllum* extract powder; and
- (f) isolating and refining further as needed.

Ex. 1020 ¶¶ 80–87.

Petitioner contends that applying Huh's GP extraction process results in a composition meeting the claimed pharmaceutical composition comprising damulin A and damulin B at the recited concentrations. *See* Pet. 64–66. Specifically, Petitioner contends that “[e]xperimental data shows that when an extraction is prepared according to the process of Huh and the butanol evaporation of step (d) is performed by boiling the butanol, the amount of damulin A in the resulting extract is 0.51% or greater.” Pet. 65 (citing Ex. 1016, 12). Petitioner acknowledges that it was only by raising the temperature to maintain a constant boil during the evaporation process that it was determined that damulin A was present within the recited concentration. *See* Pet. 65 (citing Ex. 1016, 4, 12).

Patent Owner contends that “Petitioner admits that Huh does not disclose or suggest damulin A or B or the Claimed Concentrations.” Prelim. Resp. 58 (citing Pet. 3, 64–65). Patent Owner contends that “Petitioner admits: ‘Huh does not explain how butanol should be evaporated at step (d).’” *Id.* at 59 (citing Pet. 65); *see also id.* at 61 (“Petitioner fails to provide prior art teaching Petitioner’s [experimental] conditions.”).

On the current record, we agree with Patent Owner that Petitioner has not sufficiently established that following Huh’s extraction procedure as disclosed in the published application would necessarily result in a product within the limits recited in claim 8.

Huh does not provide sufficient detail with respect to their GP extraction methods. *See* Prelim. Resp. 59–60. This is supported by the testimony of Dr. Lee, Petitioner’s Declarant, explaining that optimization of Huh’s experimental protocol was required in order to determine the appropriate conditions for extraction. *See* Ex. 1017 ¶ 6 (Example 1 of Ex. 1020 “is silent on the specific conditions such as temperature, hour and mixture ratio etc., and thus I performed preliminary experiments in order to find appropriate process conditions for the experiments.”). Petitioner’s Experimental Report-2 showing damulin A at a concentration of 0.75%, therefore, is a result flowing from Dr. Lee’s optimization of experimental conditions (*see* Ex. 1017 ¶¶ 6–11) and not a natural result flowing from Huh’s disclosure (Ex. 1020 ¶¶ 81–87).

Additionally, we agree with Patent Owner that Petitioner does not provide any indication with respect to the levels of damulin B in the Experimental Report-2. Prelim. Resp. 58–59. For these reasons, we agree with Patent Owner that Petitioner has not sufficiently shown that the

damulin A and damulin B concentration in Huh's GP extract are within the claimed ranges of claim 8.

Based on that apparent deficiency, with respect to Huh's GP extraction method, Petitioner has not shown sufficiently that the Petition demonstrates that there is a reasonable likelihood that claims 8, 9, and 12 are unpatentable over Huh.

J. *Other Issues*

Patent Owner argues that "Petitioner has not shown that there are significant and material differences" between Kim 460 and Ex. 1019.

Prelim. Resp. 17. Indeed, Petitioner does not address Ex. 1019. *Id.*

According to Patent Owner, "[b]oth Kim 460 and Ex. 1019 disclose substantially the same method of heating ginseng in an autoclave." *Id.*

Patent Owner appears to present a 35 U.S.C. § 325(d) argument with respect to Kim 460. Petitioner, however, presented at least one additional ground of unpatentability that does not rely on Kim 460; and for the reasons discussed above (*see* § II.G) we determined that Petitioner has demonstrated sufficiently that, there is a reasonable likelihood that at least one of the challenged claims of the '786 patent is unpatentable and rendered obvious over the combination of WO 178 and Razmovski. Because we are instituting on another ground we need not reach Patent Owner's argument with respect to Kim 460.

III. CONCLUSION

After considering the evidence and arguments presented in the current record, Petitioner has demonstrated a reasonable likelihood of success in proving that the challenged claims of the '786 patent are unpatentable. We therefore institute trial on all challenged claims under each of the grounds

raised in the Petition. *See PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (Indicating that a decision whether to institute an *inter partes* review “require[s] a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition.”); 37 C.F.R. § 42.108(a). At this stage of the proceeding, we have not made a final determination with respect to the patentability of any of the challenged claims.

Any argument not raised in a timely Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed waived even if asserted in the Preliminary Response. *See In re NuVasive, Inc.*, 842 F.3d 1376, 1380–81 (Fed. Cir. 2016) (holding Patent Owner waived an argument addressed in the Preliminary Response by not raising the same argument in the Patent Owner Response). In addition, nothing in this Decision authorizes Petitioner to supplement information advanced in the Petition in a manner not permitted by the Board’s Rules.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–13 of the ’786 patent is instituted with respect to the grounds set forth in the Petition; and

FURTHER ORDERED, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), that the *inter partes* review of the ’786 patent shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

IPR2022-00998
Patent 8,357,786 B2

FOR PETITIONER:

Kevin Raudebaugh
Jinchul Hong
AMPACC LAW GROUP, PLLC
kwr@ampacc.com
jch@ampacc.com

FOR PATENT OWNER:

Aydin Harston
ROTHWELL, FIGG, ERNST & MANBECK, P.C.
aharston@rfem.com