

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AZURITY PHARMACEUTICALS, INC.,
Petitioners,

v.

HELSINN HEALTHCARE S.A.,
Patent Owner.

IPR2025-00948
Patent 9,943,515 B2

Before MICHAEL J. FITZPATRICK, SHERIDAN K. SNEDDEN, and
CHRISTOPHER J. PAULRAJ, *Administrative Patent Judges*.

FITZPATRICK, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Petitioner, Azurity Pharmaceuticals, Inc., filed a Petition to institute an *inter partes* review of all twenty-three claims of U.S. Patent No. 9,943,515 B2 (Ex. 1003, “the ’515 patent”). Paper 2 (“Pet.”). Patent Owner, Helsinn Healthcare S.A., filed a Preliminary Response. Paper 10 (“Prelim. Resp.”).

Patent Owner also filed a discretionary denial brief, and Petitioner filed an opposition thereto. Papers 7 and 8. On September 19, 2025, then Acting Director Stewart denied discretionary denial and referred the Petition to the Board. Paper 11, at 3–4.

Institution of an *inter partes* review requires that “the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). Determining whether to institute has been delegated to the Board. *See* 37 C.F.R. § 42.4(a) (“The Board institutes the trial on behalf of the Director.”).

Upon consideration of the Petition and the Preliminary Response, and for the reasons explained below, we determine that there is a reasonable likelihood that Petitioner would prevail with respect to at least one claim. Accordingly, we grant the Petition.

II. BACKGROUND

A. *Real Parties in Interest*

Each party identifies itself as the sole real party in interest. Pet. 69; Paper 4, at 1. At this stage, neither party has raised a dispute regarding the requirement to identify a real party-in-interest.

B. Related Matters

The parties identify four petitions for *inter partes* reviews of related patents. Pet. 69; Paper 4, at 1. Those four petitions, along with the instant petition, and the subject patents are:

IPR2025-00945 (regarding Patent 8,623,826 B2);
IPR2025-00946 (regarding Patent 9,186,357 B2);
IPR2025-00947 (regarding Patent 9,186,357 B2);
IPR2025-00948 (regarding Patent 9,943,515 B2); and
IPR2025-00949 (regarding Patent 10,828,297 B2).

C. The '515 Patent (Ex. 1003)

The '515 patent is titled “Compositions and Methods for Treating Centrally Mediated Nausea and Vomiting.” Ex. 1003, code (54). The claimed invention “relates to the use of centrally acting NK₁ antagonists to treat nausea and vomiting, particular nausea and vomiting induced by highly emetogenic chemotherapy, and to the treatment of such nausea and vomiting over multiple consecutive days.” Ex. 1003, 1:25–29.

The term NK₁ (or NK-1) antagonists refers to neurokinin-1 receptor antagonists. *See, e.g.*, Ex. 1009 ¶23.¹ One such NK₁ antagonist is aprepitant. According to the '515 patent,

NK₁ antagonists have . . . recently emerged as a tool for combating nausea and vomiting from emetogenic medical procedures. Most recently, aprepitant was approved by the Food and Drug Administration (“FDA”) for use in combination with other anti-emetic agents for the prevention of

¹ Exhibit 1009 is a declaration by Stephen J. Peroutka, M.D., Ph.D. Ex. 1009 ¶2.

nausea and vomiting from moderately and highly emetogenic chemotherapy. However, it quickly became apparent that aprepitant's effect was limited principally to vomiting—not nausea—and that aprepitant did not provide as much benefit during the acute phase of CINV [(i.e., chemotherapy-induced nausea and vomiting²)].

Ex. 1003, 2:18–28.

“Netupitant is another selective NK₁ receptor antagonist under development by Helsinn Healthcare.” *Id.* at 3:14–15. The '515 patent acknowledges that netupitant was known in the art. *See id.* at 3:37–39 (“Methods of synthesizing and formulating netupitant and its prodrugs are described in U.S. Pat. Nos. 6,297,375, 6,719,996 and 6,593,472 to Hoffmann La Roche.”). The named inventors of the '515 patent, however, claim to have discovered that “netupitant is active against nausea.” *Id.* at 4:56–57. In their words:

After extensive testing into the clinical effects of netupitant, it has unexpectedly been discovered that netupitant is active against nausea, and that a single dose of netupitant is able to treat nausea and vomiting in response to highly and moderately emetogenic chemotherapy for five consecutive days. It has also been discovered, quite unexpectedly, that netupitant exhibits unique binding habits to NK₁ receptors in the brain. In particular, it has been discovered that netupitant binds to NK₁ receptors in the striatum in a long-lasting manner, and that less than 20 or 30% of netupitant is released from striatum NK₁ receptors even ninety-six hours after administration. This is

² *See* Pet. 6 (referring to “chemotherapy-induced nausea and vomiting (CINV)”); Prelim. Resp. 1 (same).

in stark contrast to aprepitant, in which receptor binding drops swiftly over time, and must be dosed repeatedly if emesis control is desired throughout the delayed phase; and which shows no meaningful effect against nausea.

Id. at 4:55–5:3.

The '515 patent's filing date is January 21, 2016. Ex. 1003, code (22). However, it claims priority to multiple applications, the earliest of which is a provisional application filed November 18, 2009. Ex. 1003, 1:9–17; *see also id.* at codes (60), (63). Neither party directly addresses whether the challenged claims are entitled to an effective filing date prior to the actual filing date. However, the Petition challenges the claims as if they were effectively filed November 18, 2009. For example, the Petition defines the level of skill as of 2009. Pet. 9. Further, as discussed below, each asserted prior art reference indicates it was either patented or published more than one year before November 18, 2009.

D. Challenged Claims

The Petition challenges all twenty-three claims of the '515 patent, of which claims 1 and 11 are independent. Claim 11 is illustrative and reproduced below with paragraphing added.

11. A method of treating nausea and vomiting in response to an emesis-inducing event for a period of five consecutive days in a patient in need thereof, comprising

administering to said patient netupitant or a pharmaceutically acceptable salt thereof, in a therapeutically effective amount which is effective to treat nausea and vomiting during the acute and delayed phases of emesis, wherein said therapeutically effective amount of netupitant or pharmaceutically acceptable salt thereof is administered on day one of said five consecutive days, no further netupitant or

pharmaceutically acceptable salt thereof is administered during said five consecutive days, and said single dose of netupitant or pharmaceutically acceptable salt thereof if effective to treat said nausea and vomiting for said five consecutive days.

Ex. 1003, 23:1–14 (paragraphing added).

E. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
11–17, 19–23	103	Herrstedt, ³ Bös, ⁴ Herrington ⁵
1–10, 18	103	Herrstedt, Bös, Hargreaves, ⁶ Herrington

The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”), included amendments to 35 U.S.C. §§ 102 and 103 that became effective March 16, 2013. These amendments apply to applications (and patents issued thereon) that contained at any time—(A) a claim that has an effective filing date on or after March 16, 2013 or (B) a specific reference under 35 U.S.C. §§ 120, 121, or 365(c) to any patent or application that contains or contained at any time such a claim. *Id.* at § 3(n).

³ J. Herrstedt et al., *Anti-Emetic Therapy in Cancer Chemotherapy: Current Status*, 101 BASIC & CLINICAL PHARMACOLOGY & TOXICOLOGY 143–150 (2007) (Ex. 1010).

⁴ US 6,297,375 B1, issued October 2, 2002 (Ex. 1014).

⁵ J.D. Herrington et al., *Randomized, Placebo-controlled, Pilot Study Evaluating Aprepitant Single Dose Plus Palonosetron and Dexamethasone for the Prevention of Acute and Delayed Chemotherapy-induced Nausea and Vomiting*, 112 CANCER 2080–87 (March 7, 2008) (Ex. 1016).

⁶ R. Hargreaves, *Imaging Substance P Receptors (NK1) in the Living Human Brain Using Positron Emission Tomography*, 63(11) J. CLINICAL PSYCHIATRY 18–24 (2002) (Ex. 1012).

Based on the evidence of record, each of the asserted references is prior art to the challenged claims under either version of § 102. More specifically, each reference indicates that it was either patented or published more than one year before November 18, 2009. *See supra*, nn. 2–4. Thus, each reference is prior art under either version of section 102. *See pre-AIA* 35 U.S.C. § 102(b) (“A person shall be entitled to a patent unless . . . the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.”); *AIA* 35 U.S.C. § 102(a)(1) (“A person shall be entitled to a patent unless . . . the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.”). Nor does Patent Owner argue that any of the asserted references do not constitute prior art to the challenged claims. *See generally* Prelim. Resp.

III. ANALYSIS OF THE ASSERTED GROUNDS

A. Level of Ordinary Skill in the Art

In determining whether an invention would have been obvious at the time it was made, we consider the level of ordinary skill in the pertinent art at the time of the invention. *Graham v. John Deere of Kan. City*, 383 U.S. 1, 17 (1966). “The importance of resolving the level of ordinary skill in the art lies in the necessity of maintaining objectivity in the obviousness inquiry.” *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991). The “person having ordinary skill in the art” is a hypothetical construct, from whose vantage point obviousness is assessed. *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

Petitioner contends a person of ordinary skill in the art (“POSA”) would be someone “skilled in *one of* ‘clinical medicine, medical oncology, radiation oncology, oncology nursing, statistics, pharmacy, medical policy and decision making, and pharmacology.’” Pet. 8–9 (emphasis added) (quoting Ex. 1013, 20⁷). Petitioner further contends:

In 2009, such professionals had advanced degrees in pharmacology, medicine, or allied fields, and would have worked in consultation with other specialists in these fields, and would have practical knowledge and experience about metabolism studies, in-vitro and in-vivo testing, formulation, and combination therapy.

Pet. 9.

Patent Owner “disagrees” with Petitioner’s contention “to the extent [it] does not require experience in the field of oncology, including work experience with cancer supportive care medications.” Prelim. Resp. 12. Patent Owner also proposes its own definition, arguing:

A POSA at the time of the claimed invention was actively involved in the field of oncology and, more specifically, supportive cancer care, which involves a number of disciplines and requires collaborative teamwork among persons with relevant experience. The POSA could have an advanced degree (*e.g.*, Ph.D., M.D., M.S., MSN, DNP, or equivalent) in a relevant field (*e.g.*, oncology) with at least three years of experience in oncology, including the treatment of nausea and vomiting with supportive cancer care medications

⁷ *Prevention of chemotherapy and radiotherapy-induced emesis: results of the 2004 Perugia International Antiemetic Consensus Conference*, 17 ANNALS OF ONCOLOGY 20–28 (2006) (Ex. 1013).

in cancer patients undergoing chemotherapy. More education can substitute for practical experience and *vice versa*.

Id.

At this stage, we need not resolve the parties' dispute with regard to the requisite level of skill in the art, as our analysis would be the same under either party's definition of a POSA. We note, however, that Petitioner's definition seems to be overly broad insofar as it would only require the POSA to be skilled in one of several broad fields, including "statistics" and "medical policy and decision making," that do not directly relate to the claimed subject matter. At the same time, we do not agree with Patent Owner that the POSA needs specific clinical experience in the field of oncology. The claimed subject matter relates to the treatment of a side-effect associated with cancer therapy (CINV), and not the cancer itself. We also recognize that the prior art and the '357 patent itself reflect the level of skill in the art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) ("[T]he absence of specific findings on the level of skill in the art does not give rise to reversible error where the prior art itself reflects an appropriate level and a need for testimony is not shown.").

We further find, based on the present record, that both parties' experts are qualified to testify from the perspective of a POSA in this proceeding. *See* Ex. 1009 ¶¶ 1–7 (Dr. Peroutka's qualifications); Ex. 2069 ¶¶ 8–15 (Dr. Navari's qualifications); *Kyocera Senco Indus. Tools Inc. v. Int'l Trade Comm'n*, 22 F.4th 1369, 1377 (Fed. Cir. 2022) ("[T]o be qualified to offer expert testimony on issues from the vantage point of an ordinarily skilled artisan in a patent case, an expert must at a minimum possess ordinary skill in the art."). Even if some specific experience with regard to the treatment

of CINV is required, Dr. Peroutka appears to have published in that field. *See, e.g.*, Ex. 1020 at 10 (publication 16: article on “Combination antiemetics” in Cancer Treatment Reports), 11 (publication 37: article on “Neurotransmitter receptor binding studies predict antiemetic efficacy and side effects” in Cancer Treatment Reports), 13 (publication 51: article on “Chemotherapeutic agents do not interact with neurotransmitter receptors” in Cancer Chemotherapy and Pharmacology).

B. Claim Construction

In an *inter partes* review, claim terms “shall be construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b), 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).

Petitioner proposes several constructions. Pet. 9–10. Patent Owner does not dispute any of Petitioner’s constructions but argues that they are “unnecessary to resolve the parties’ disputes here.” Prelim. Resp. 13. We address each below.

First, Petitioner proposes that “therapeutically effective amount” (recited in both independent claims) means: an amount sufficient to elicit the desired biological response. Pet. 9 (citing Ex. 1003, 8:13–15). The cited portion of the Specification clearly supports such a construction. Ex. 1003, 8:13–15 (“As used herein, ‘therapeutically effective amount’ refers to an amount sufficient to elicit the desired biological response.”). We adopt it.

Second, Petitioner proposes that “the word *if* in claims 1 and 11 appears from context to mean ‘is’.” *Id.* (citing *Ex parte Tanksley*, 26 USPQ2d 1384, 1387 (BPAI 1991)). Both of the independent claims conclude with the following clause: “and said single dose of netupitant or pharmaceutically acceptable salt thereof *if* effective to treat said nausea and vomiting for said five consecutive days.” (Emphasis added). The word “if” cannot *mean* “is,” as Petitioner literally proposes. Pet. 9. However, we understand Petitioner to be arguing implicitly that (1) “if” was a typographical or other error in the independent claims and (2) “is” was intended in its place. Such is a reasonable position in the context of the challenged claims. On the instant record, with no argument to the contrary by Patent Owner, we construe claims 1 and 11 such that the word “is” was intended in lieu of the word “if” in the last clause of each claim. *Cf. Canatex Completion Sols., Inc., v. Wellmatics, LLC*, No. 2024-1466, 2025 WL 3153362, at *5 (Fed. Cir. Nov. 12, 2025) (“[W]e have ruled that a district court may correct obvious minor typographical and clerical errors in patents.”) (cleaned up; citations omitted)).

Third, Petitioner proposes a construction for “minimum effective dose of dexamethasone.” Pet. 10. That term appears nowhere in the challenged claims. Accordingly, we do not interpret the term.

Finally, Petitioner proposes construing the following language appearing in claim 1: “administering to said patient netupitant or a pharmaceutically acceptable salt thereof, in a therapeutically effective amount . . . which enters the systemic circulation, crosses the blood brain barrier and occupies 70% or more of NK₁ receptors in the striatum seventy-two hours after said administration.” Pet. 10 (emphasis added).

Specifically, Petitioner proposes that the italicized language, as introduced by the word “which,” denotes inherent properties (and not further limitations) resulting from the administering of the drug in a therapeutically effective amount. *Id.* On the instant record, with no argument to the contrary by Patent Owner, we agree with Petitioner. However, we do not explicitly address claim 1 below. Instead, the focus of our institution analysis is independent claim 11.

C. The Asserted References

i. Herrstedt (Ex. 1010)

Petitioner argues that Herrstedt is a journal article published in 2007, as shown on the face of Exhibit 1010. Pet. 11. Patent Owner does not dispute that Herrstedt is prior art to the challenged claims.

Herrstedt is titled *Anti-Emetic Therapy in Cancer Chemotherapy: Current Status*. Ex. 1010, 1. It focuses on two classes of anti-emetics: serotonin₃-receptor antagonists and NK₁ receptor antagonists. *Id.* at Abstr. According to Herrstedt:

The serotonin₃-receptor antagonists, the first group of drugs developed specifically as anti-emetics, have significantly improved the prophylaxis of chemotherapy-induced emesis especially in combination with a corticosteroid. The improvement in the prophylaxis of nausea with this combination is however modest. A new group of anti-emetics, the neurokinin₁-receptor antagonists, has now been developed, and the first drug, aprepitant, was marketed in 2003. Aprepitant increases the effect of a serotonin₃-receptor antagonist plus a corticosteroid against acute emesis induced by highly or moderately emetogenic

chemotherapy and aprepitant is also active in the protection against delayed emesis.

Id. Serotonin is also known as 5-hydroxytryptamine or 5-HT. Hence, “5-HT₃-receptor antagonist” and “serotonin₃-receptor antagonist” are synonymous. Ex. 1009 ¶79.

Herrstedt describes studies of a combination therapy that demonstrated that the addition of aprepitant was beneficial to prevent CINV. *See, e.g.*, Ex. 1010, 146. Further, “[t]he combination of aprepitant and oral dexamethasone results in a two-time increase in the AUC [(i.e., area under the curve)] of dexamethasone indicating an inhibition of aprepitant on dexamethasone metabolism.” *Id.* at 147.

ii. Bös (Ex. 1014)

Bös is a United States patent issued October 2, 2001. Ex. 1014, code (45). Patent Owner does not dispute that Bös is prior art to the challenged claims.

Bös explains that substance P is naturally present in the body, binds to NK₁ receptors, and is associated with numerous conditions. *Id.* at 1:17–67. Bös teaches using NK₁ antagonists to inhibit such conditions. *Id.* at 1:35–67. Of particular relevance here, Bös teaches using NK₁ antagonists for “mediation of the emetic reflex” and “for the treatment of motion sickness and for treatment [of] induced vomiting,” and, most relevantly, for “the reduction of cisplatin⁸-induced emesis.” *Id.* at 1:27, 1:59–64.

⁸ Cisplatin is chemotherapeutic agent. *See* Ex. 1003, (“‘Highly emetogenic chemotherapy’ refers to chemotherapy having a high degree of emetogenic potential, and includes chemotherapy based on carmustine, *cisplatin*,

Although Bös does not refer to it as “netupitant,” Bös identifies and describes netupitant by its chemical formula, identifies it as “compound Ib,” and teaches that it has “valuable therapeutic properties as a highly selective antagonist of the Neurokinin 1 (NK-1, substance P).” *Id.* at 14:9–38. Bös tested netupitant in ferrets and observed that it “completely blocked the emesis induced by the emetogens.” *Id.* at 19:10–20.

iii. Herrington (Ex. 1016)

Petitioner argues that Herrington is a journal article published in 2008, as shown on the face of Exhibit 1016. Pet. 13–14. Patent Owner does not dispute that Herrington is prior art to the challenged claims.

Herrington is titled *Randomized, Placebo-controlled, Pilot Study Evaluating Aprepitant Single Dose Plus Palonosetron and Dexamethasone for the Prevention of Acute and Delayed Chemotherapy-induced Nausea and Vomiting*. Ex. 1016, 1. Herrington describes clinical trials demonstrating that a single dose on day-one of a therapeutically effective amount of NK₁ antagonist is as effective as multi-day administration of the same. *See* Ex. 1016, Abstr. (“From this pilot study of patients who were receiving palonosetron, aprepitant, and dexamethasone for highly emetogenic chemotherapy, a single dose of aprepitant displayed similar effectiveness compared with 3-day aprepitant.”).

iv. Hargreaves (Ex. 1012)

Hargreaves is not critical to this Decision because we assess below only the Ground 1 challenge to independent claim 11. Nonetheless, we

cyclophosphamide > 1500 mg/m², dacarbazine, dactinomycin, mechlorethamine, and streptozotocin.” (emphasis added)).

briefly discuss its teachings, as it will be relevant to Ground 2 during the instituted *inter partes* review.

Petitioner argues that Hargreaves is a journal article published in 2002, as shown on the face of Exhibit 1012. Pet. 13. Patent Owner does not dispute that Hargreaves is prior art to the challenged claims.

Hargreaves is titled *Pathophysiology of Depression: The Emerging Role of Substance P*. Ex. 1012. Hargreaves teaches that “clinical studies have demonstrated that treatment with . . . aprepitant . . . significantly improves depression symptoms and reduces the incidence of chemotherapy-induced *nausea* and vomiting.” *Id.* at Abstr. Hargreaves describes using positron emission tomography (PET) “to establish the correlation between dose [of aprepitant], receptor occupancy, and the observed clinical effect.” *Id.* Hargreaves teaches an approximately 75% or greater NK₁-receptor occupancy was associated with therapeutic doses that blocked emesis. *Id.* at 23 (Fig. 6B).

D. Ground 1: Claims 11–17 and 19–23 as Obvious over Herrstedt, Bös, and Herrington

Petitioner contends that claims 11–17 and 19–23 would have been obvious over Herrstedt, Bös, and Herrington. Pet. 15–30.

A claim is unpatentable “if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.” 35 U.S.C. § 103. “Obviousness is a question of law based on underlying facts.” *MobileMedia Ideas LLC v. Apple Inc.*, 780 F.3d 1159, 1167 (Fed. Cir. 2015). The underlying facts include “(i) the scope and

content of the prior art, (ii) the differences between the prior art and the claimed invention, (iii) the level of ordinary skill in the field of the invention, and (iv) any relevant objective considerations of nonobviousness.” *Id.* (citing *Graham v. John Deere of Kan. City*, 383 U.S. 1, 17–18 (1966)). An additional underlying fact is whether there was a reason to combine prior art teachings when so asserted. *Id.*; *see also KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418–19 (2007) (“[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.”).

As discussed below, we determine that Petitioner has a reasonable likelihood of succeeding in its challenge at least as to independent claim 11.

i. Independent Claim 11

Independent claim 11 is directed to “[a] method of treating nausea and vomiting in response to an emesis-inducing event for a period of five consecutive days in a patient in need thereof.” Ex. 1003, 23:1–3. It recites a single step:

administering to said patient netupitant or a pharmaceutically acceptable salt thereof, in a therapeutically effective amount which is effective to treat nausea and vomiting during the acute and delayed phases of emesis, wherein said therapeutically effective amount of netupitant or pharmaceutically acceptable salt thereof is administered on day one of said five consecutive days, no further netupitant or pharmaceutically acceptable salt thereof is administered during said five consecutive days, and said single dose of netupitant or

pharmaceutically acceptable salt thereof [is] effective to treat said nausea and vomiting for said five consecutive days.

Id. at 23:3–14.

Herrstedt teaches adding a single dose of aprepitant to a combination drug therapy of a serotonin₃-receptor antagonist (e.g., palonosetron) and a corticosteroid (e.g., dexamethasone) for preventing acute and delayed CINV. Ex. 1010, Title and Abstr. Petitioner argues that it would have been obvious to substitute netupitant, a more recently discovered NK₁ antagonist, for Herrstedt’s aprepitant in view of Bös. Pet. 18–19 (citing Ex. 1014 *passim*; Ex. 1009 ¶¶516–519). Petitioner further argues that it would have been obvious to administer only a single dose of netupitant on the first of five consecutive days because, Herrington “confirms” (as Herrstedt suggests) “that a single dose of NK₁ antagonist on day 1 renders further doses in the 5-day period unnecessary.” *Id.* at 20 (citing Ex. 1016, 1).⁹

Patent Owner argues that the Petition “Applies the Wrong Legal Framework” because it “begins with Helsinn’s invention, and then works backwards by cobbling together the prior art so as to arrive at the claimed invention[.]” Prelim. Resp. 14. Thus, Patent Owner argues, “Azurity’s approach is emblematic of impermissible hindsight and must fail for this reason alone.” *Id.* at 15.

⁹ The Petition actually cites to Exhibit 1017, but that is a typographical error. Pet. 20. In the sentence at issue, the Petition expressly refers to “Herrington,” which is Exhibit 1016, and it is Exhibit 1016 that contains the language the Petition proceeds to quote: “From this pilot study of patients who were receiving palonosetron, aprepitant, and dexamethasone for highly emetogenic chemotherapy, a single dose of aprepitant displayed similar effectiveness compared with 3-day aprepitant.” Ex. 1016, 1.

Patent Owner’s specific critique in this regard is that the Petition analyzes *only* whether the claimed invention would have been obvious and not whether *other* methods of treating CINV that are not covered by the challenged claims also would have been obvious. *See id.* at 17 (“Contrary to Azurity’s assertions, the obviousness question here cannot be narrowly framed to focus only on whether it would have been obvious to a POSA [to] substitute netupitant for aprepitant in the three-drug regimen.”). According to Patent Owner, “A POSA in November 2009 Had Many Potential Pathways for Attempting to Develop an Improved Treatment for CINV That Allowed for Control of Nausea.” *Id.* at 19. “For example, [Patent Owner argues,] one possible pathway for a POSA to consider would have been adding a **fourth** drug to the three-drug regimen to control nausea instead of substituting for individual drugs (*e.g.*, aprepitant) in that regimen.” *Id.* at 19–20; *see also id.* at 21 (“For example, a POSA could have considered adding other drugs, like gabapentin and cannabinoids, from other, different drug classes to the three-drug regimen for controlling nausea.”), 23 (“Azurity, however, fails to consider any of the[] alternative NK-1 receptor antagonists that were known by November 2009—let alone their advantages or shortcomings—and instead contends that a POSA would have zeroed in on netupitant.”). Patent Owner concludes that “Azurity’s lack of consideration of these alternate paths, coupled with its singular focus on netupitant, underscores that its obviousness analysis is infected by impermissible hindsight.” *Id.* at 22.

We are not persuaded by these arguments. The fact that multiple solutions to the problem of treating CINV may have been obvious is not probative that the combination proposed by Petitioner is non-obvious. The

law expressly contemplates that there can be more than one obvious solution to the same problem. Indeed, an inferior solution can still be obvious even when a superior solution is also available. *See In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012) (“[J]ust because better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes.”); *Bayer Pharma AG v. Watson Lab'ys, Inc.*, 874 F.3d 1316, 1327 (Fed. Cir. 2017) (“When there are only two possible formulations and both are known in the art at the time, the fact that there may be reasons a skilled artisan would prefer one over the other does not amount to a teaching away from the lesser preferred but still workable option.”). Further, obviousness “does not require that the motivation be the *best* option, only that it be a *suitable* option from which the prior art did not teach away.” *Par Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1197–98 (Fed. Cir. 2014).

Patent Owner’s impermissible hindsight arguments are additionally unpersuasive because Patent Owner fails to rebut Petitioner’s reason for substituting netupitant for aprepitant. *See In re Cree, Inc.*, 818 F.3d 694, 702 n.3 (Fed. Cir. 2016) (Explaining that a hindsight argument is of no moment in the face of sufficient reason to combine the references). Petitioner’s witness, Dr. Peroutka, testifies that, because Bös teaches a POSA that netupitant has “**valuable therapeutic properties** as a **highly selective** antagonist of the Neurokinin 1 (NK-1, substance P),” it would have been obvious to substitute it “in place of the existing NK₁ receptor antagonist (aprepitant) in the combination treatment disclosed in Herrstedt.” Ex. 1009 ¶507 (quoting Ex. 1014, 14:31–34). Patent Owner does not dispute that aprepitant and netupitant were both known NK₁ receptor antagonists, and it is obvious to those skilled in the art to substitute one

known equivalent for another. *See In re Omeprazole Patent Litigation*, 483 F.3d 1364, 1374 (Fed. Cir. 2007) (“[T]his court finds no . . . error in [the] conclusion that it would have been obvious to one skilled in the art to substitute one ARC [alkaline reactive compound] for another.”).

Further, the Petition identifies explicit teachings by Bös that supports the obviousness of using netupitant in lieu of aprepitant in Herrstedt’s therapy for preventing CINV. First, Bös teaches that NK₁ antagonists are useful for “mediation of the emetic reflex” and “for the treatment of motion sickness and for treatment [of] induced vomiting,” and, most relevantly, for “the reduction of cisplatin-induced emesis.” Ex. 1014, 1:27, 1:59–64 (cited at Pet. 12). Second, Bös specifically identifies and describes netupitant as an NK₁ antagonist and teaches that it has “valuable therapeutic properties as a highly selective antagonist of the Neurokinin 1 (NK-1, substance P).” *Id.* at 14:9–38 (cited at Pet. 12–13).

Patent Owner argues that, even if the prior art teaches using netupitant, Petitioner fails to show that the prior art teaches or renders obvious administering netupitant to a patient *on only the first of five consecutive days*, as specified in claim 11. Prelim. Resp. 26–30. More specifically, Patent Owner argues “neither [Herrington nor Bös] discloses any dosing regimen for netupitant, much less that administering a **single dose** of netupitant is effective in treating **nausea** and vomiting for five consecutive days after an emesis-inducing event, as claimed.” *Id.* at 27. This is so, Patent Owner continues, because “Bös is silent on how many times netupitant should be administered,” and “Herrington does not even mention netupitant, let alone disclose any dosing for netupitant.” *Id.* at 27–28.

We are not persuaded by these arguments because Petitioner's challenge is based on a combination of the asserted references, which also includes Herrstedt. As to the instant limitation, for example, Petitioner explains as follows:

The combined teachings of Herrstedt and Bös suggest a single dose of netupitant is administered on the first of said five consecutive days, with no further netupitant during the five consecutive days, would be effective to treat nausea and vomiting for the five-day period because netupitant was known to have a large half-life value, thus providing reason to omit subsequent NK₁-antagonist dosing. [Ex. 1014], 19:3–10 (functional half-life of 30 hours). EX1009, ¶522. Herrington confirms the suggestion that a single dose of NK₁ antagonist on day 1 renders further doses in the 5-day period unnecessary because Herrington teaches a single dose of aprepitant provided similar effectiveness as compared to Herrstedt's protocol of dosing aprepitant three times. EX1016 [sic, 1018¹⁰], Background (“The purpose of this pilot study was to *ascertain the effectiveness of 1-day versus 3-day aprepitant* in the prevention of acute and delayed nausea and vomiting in patients who were receiving highly emetogenic chemotherapy. . . . From this pilot study of patients who were receiving palonosetron, aprepitant, and dexamethasone for highly emetogenic chemotherapy, a *single dose of aprepitant displayed similar effectiveness compared with 3-day aprepitant.*”). Thus, a POSA would have reasonably expected a single dose of an NK₁ antagonist on day 1 would be as successful as

¹⁰ The Petition cites to Exhibit 1017, but it is clear, from both the reference to “Herrington” and the quoted content, that Exhibit 1016 was the intended exhibit.

dosing the NK₁ antagonist on multiple days.
EX1009, ¶523.

Pet. 20–21. Patent Owner’s arguments that “Bös is silent on how many times netupitant should be administered,” and “Herrington does not even mention netupitant” (Prelim Resp. 27–28) are classic examples of attacking references individually. *See In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986) (“Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references.”). Each of Bös and Herrington “must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole,” including Herrstedt. *Id.*

In addressing the actual combination proposed by Petitioner, Patent Owner argues that Petitioner “provides no basis” for why a POSA would have expected netupitant to behave similarly to aprepitant. Prelim. Resp. 28. We disagree. Petitioner’s proposed substitution of netupitant for aprepitant is supported by Bös’s teaching that NK₁ antagonists can be used for “the reduction of cisplatin-induced emesis,” and, consistent with that teaching, Bös’s further description of netupitant, in particular, as having “valuable therapeutic properties as a highly selective antagonist of the Neurokinin 1 (NK-1, substance P).” Ex. 1014, 1:59–64, 14:9–38; *see Novo Nordisk A/S v. Caraco Pharm. Lab’ys, Ltd.*, 719 F.3d 1346, 1355 (Fed. Cir. 2013) (“It is reasonable that an artisan seeking to combine a known insulin sensitizer (like metformin) with a new insulin secretagogue (like repaglinide) would base his expectations upon prior art sensitizer/secretagogue combinations.”).

Patent Owner argues, however, that “Herrington teaches that ‘*aprepitant fails to demonstrate* improved efficacy over placebo for the prevention of *nausea . . .*’” and, thus, a POSA would not have expected

netupitant to be effective against nausea. Prelim. Resp. 28–29 (quoting Ex. 1016, 2086). We are not persuaded that this argument disproves Petitioner’s reason to combine.

First, Patent Owner’s characterization of what Herrington “teaches” is an overstatement. What Herrington states is: “*According to its package insert*, aprepitant fails to demonstrate improved efficacy over placebo for the prevention of nausea (overall and significant nausea) in acute or delayed phases.” Ex. 1016, 2086 (emphasis added). And yet, despite that, Herrington teaches the POSA to use aprepitant to treat emesis caused by chemotherapy, stating:

In conclusion, the current study has demonstrated that a single dose of aprepitant 125 mg has similar effectiveness as the 3-day aprepitant regimen. These findings are similar to previous, older formulation, aprepitant studies, which compared a single dose to 5 days of aprepitant therapy. In addition, the use of a single 125 mg dose would equate to lower drug cost with similar effectiveness for highly emetogenic chemotherapy regimens. With this combination of palonosetron and aprepitant, greater than 90% of patients can be emesis-free during Days 1–5 after chemotherapy.

Id. Second, a separate reference, Herrstedt, clearly teaches the use of aprepitant for preventing CINV even though it may not be fully effective. Ex. 1010, Abstr., 146.

In any event, even if a POSA thought aprepitant was useful in preventing only chemotherapy-induced *vomiting* (“CIV”) but not

chemotherapy-induced *nausea* (“CIN”),¹¹ prior art of record (Herrstedt and Herrington) nonetheless teaches administering aprepitant to chemotherapy patients and further prior art of record (Bös) provides a reason to substitute netupitant for aprepitant.

In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. . . . [A]ny 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.

KSR Int’l Co. v. Teleflex Inc., 550 U.S. 398, 419–20 (2007). Thus, and for the sake of argument, even if a POSA would have been motivated to substitute netupitant for its anticipated efficacy in preventing CIV only (but not CIN), such would still provide an adequate reason for combining the elements in the manner claimed.

Patent Owner argues that “a POSA would not have drawn any conclusions about using a single dose of an NK-1 receptor antagonist based on Herrington because using a single dose was contrary to what the art taught a POSA at the relevant time.” Prelim. Resp. 29. This is so, according to Patent Owner, because “the Emend® (aprepitant) labelling, the relevant clinical guidelines, and Herrstedt itself taught that aprepitant is dosed over three days.” *Id.* (citing Ex. 2069 ¶¶100–102; Ex. 1010, 146). We reject the premise of Patent Owner’s argument—that a POSA would have considered only existing clinical guidelines and/or FDA-approved drug labeling.

¹¹ Herrstedt teaches the use of aprepitant for preventing CIN even though it may not be fully effective. Ex. 1010, Abstr., 146.

Rather, the POSA would have known, based on Herrington’s research, “that a single 125-mg dose of aprepitant provides similar effectiveness compared with the traditional 3-day regimen.” Ex. 1016, 2084; *see also id.* at Abstr. (“From this pilot study of patients who were receiving palonosetron, aprepitant, and dexamethasone for highly emetogenic chemotherapy, a single dose of aprepitant displayed similar effectiveness compared with 3-day aprepitant.”).

Patent Owner argues that Bös fails to support the single dose limitation based on its disclosure of netupitant having a functional half-life of 30 hours. Prelim. Resp. 29–30. In particular, Patent Owner points out that the Petition “provides no explanation regarding why or how a 30-hour half-life suggests that administering netupitant would be effective against nausea and vomiting for five consecutive days (120 hours).” *Id.* at 30. We agree that the Petition seems lacking in this regard. For example, Dr. Peroutka testifies that “netupitant was known to have a longer half-life” than aprepitant, but he cites evidence indicative of netupitant’s half-life only. Ex. 1009 ¶¶594 (citing Ex. 1014, 19:3–38). He does not cite evidence indicative of aprepitant’s half-life, from which one could compare the two.

Nonetheless, we are persuaded that Petitioner has made a sufficient showing as to the single dose limitation. We reach this preliminary determination based on Herrington’s disclosure regarding the efficacy of aprepitant single dosing coupled with the known fact that aprepitant and netupitant both acted through the same mechanism, as well as Bös’s teaching that netupitant is “a highly selective [NK₁] antagonist.” Ex. 1014, 14:33–34; Ex. 1009 ¶¶521–524 (explaining that the prior art taught that a single dose of aprepitant was effective and opining that a POSA would have

followed the same single dosing regimen when substituting Bös’s “second generation NK1 receptor antagonist—netupitant” for the benefit of “decreased costs, increased convenience, and patient preference for single administration”). A single dosing on day one can be obvious even if a POSA would have expected multiple doses to be superior. *See Mouttet*, 686 F.3d at 1334 (Fed. Cir. 2012) (“[J]ust because better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes.”); *Par Pharm.*, 773 F.3d at 1197–98 (Fed. Cir. 2014) (Obviousness “does not require that the motivation be the *best* option, only that it be a *suitable* option from which the prior art did not teach away.”).

Patent Owner argues that the Petition fails to show that there would have been a reasonable expectation of success. Prelim. Res. 30–32. In particular, Patent Owner argues that “the Petition fails to show that “a POSA would have had a reasonable expectation of success *in treating nausea* with this regimen, as required by the claims.” *Id.* at 31. This is so, according to Patent Owner, because both Herrstedt and Herrington teach that aprepitant has limited efficacy in preventing CIN. *Id.* (citing Ex. 2069 ¶¶67–68; Ex. 1016, 2084).

We are not persuaded by Patent Owner’s arguments. First, Herrstedt and Herrington both teach using aprepitant (along with a serotonin₃-receptor antagonist and corticosteroid) to treat CINV even if it is not fully effective as to CIN. Ex. 1010, Abstr.; Ex. 1016, 2080; *see also* Ex. 1012, Abstr. (“Furthermore, clinical studies demonstrated that treatment with the SP (NK₁ receptor) antagonist (SPA) *aprepitant* (also known as MK-0869) significantly improves depression symptoms and *reduces the incidence of chemotherapy-induced nausea and vomiting.*” (emphasis added)).

Second, and more importantly, Patent Owner erroneously frames the legal requirement for a reasonable expectation of success. Petitioner must show that a POSA would have had a reasonable expectation of success in combining the prior art teachings in the manner claimed. *See Life Techs. Inc. v. Clontech Labs. Inc.*, 224 F.3d 1320, 1326 (Fed. Cir. 2000) (“Reasonable expectation of success is assessed from the perspective of the person of ordinary skill in the art. That the inventors were ultimately successful is irrelevant to whether one of ordinary skill in the art, at the time the invention was made, would have reasonably expected success.”). Thus, Petitioner must show that a POSA would have had a reasonable expectation of success in modifying Herrstedt’s combination therapy for treating CINV by substituting netupitant for aprepitant and administering an effective dose of netupitant on day 1 but not on days 2 through 5. Framed properly, the record evidence shows adequate support for a reasonable expectation of success. The POSA would need only substitute one known NK₁ antagonist for another, and the record supports that she would know how to dose it. *See* Ex. 1014, 42:5–11 (Bös teaching a dosing range for netupitant); *see also* Ex. 1009 ¶¶517–518 (opining as to dosing and reasonable expectation of success).

In fact, Patent Owner does not identify any obstacle a POSA might encounter in carrying out the proposed modification. Prelim. Resp. 30–32. Rather, Patent Owner disputes that a POSA would *attempt* to carry out the proposed modification because she would not have expected the netupitant to prevent CIN. However, as discussed above, the prior art taught treating CINV with aprepitant, a known NK₁ antagonist. Netupitant was another known NK₁ antagonist. The Petition demonstrates sufficiently, at least for

institution purposes, both a reason to combine the prior art and a reasonable expectation of success.

There is a reasonable likelihood of Petitioner prevailing on Ground 1 as to claim 11.

ii. Dependent Claims 12–17 and 19–23

In *SAS Institute, Inc. v. Iancu*, 138 S. Ct. 1348 (2018), the Supreme Court held the following:

Section 314(a) [of Title 35] does not require the Director to evaluate every claim individually. Instead, it simply requires him to decide whether the petitioner is likely to succeed on “at least 1” claim. Once that single claim threshold is satisfied, it doesn’t matter whether the petitioner is likely to prevail on any additional claims; the Director need not even consider any other claim before instituting review. Rather than contemplate claim-by-claim institution, then, the language anticipates a regime where a reasonable prospect of success on a single claim justifies review of all.

SAS, 138 S. Ct. at 1356; *see also* 37 C.F.R. § 42.108(a). We have already determined that the Petition satisfies the single-claim threshold of § 314(a). We discern no reason to discuss further these additional claims.

E. Ground 2: Claims 1–10 and 18 as Obvious over Herrstedt, Bös, Hargreaves, and Herrington

We have already determined that the Petition satisfies the single-claim threshold of § 314(a). We discern no reason to discuss further this additional ground. *SAS*, 138 S. Ct. at 1356; *see also* 37 C.F.R. § 42.108(a).

IV. CONCLUSION

For the reasons discussed above, we are persuaded that Petitioner has demonstrated a reasonable likelihood of prevailing in establishing that at least one of the challenged claims is unpatentable. 35 U.S.C. § 314(a).

V. ORDER

Accordingly, it is:

ORDERED that the Petition is granted and an *inter partes* review is hereby instituted as to all twenty-three claims of U.S. Patent No. 9,943,515 B2; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this decision.

IPR2025-00948
Patent 9,943,515 B2

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