

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AZURITY PHARMACEUTICALS, INC.,
Petitioner.

v.

HELSINN HEALTHCARE S.A.,
Patent Owner.

IPR2025-00946
Patent 9,186,357 B2

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

PAULRAJ, *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 and Summary*

Azurity Pharmaceuticals, Inc. (“Petitioner”) filed a Petition requesting *inter partes* review of claims 2–4, 11–16, 40–42, and 52–62 of U.S. Patent Number 9,186,357 B2 (Ex. 1002, “the ’357 patent”). Paper 2 (“Petition” or “Pet.”). Helsinn Healthcare S.A. (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 11 (“Prelim. Resp.”).

We have the authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314; 37 C.F.R. §42.4(a). We may not institute an *inter partes* review “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a).

In this decision, we address the merits of the issues raised by the parties regarding independent claims 2 and 4 of the ’357 patent. 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 challenged claim of the ’357 patent is unpatentable, we institute an *inter partes* review of all challenged claims based on the grounds set forth in the Petition.

B. *Real Parties in Interest*

Petitioner identifies Azurity Pharmaceuticals, Inc. as the real party-in-interest (“RPI”). Pet. 62. Patent Owner identifies Helsinn Healthcare S.A. as the RPI. Paper 5, 1. At this stage, neither party has raised a dispute regarding the requirement to identify an RPI.

C. Related Matters

The parties identify the following concurrently-filed *inter partes* review proceedings as related matters: IPR2025-00945 (challenging claims 1–25 of Patent 8,623,826), IPR2025-00947 (challenging claims 1, 5–10, 17–39, and 43–51 of the ’357 patent), IPR2025-00948 (challenging claims 1–23 of Patent 9,943,515), and IPR2025-00949 (challenging claims 1–23 of Patent 10,828,297). Pet. 62; Paper 5, 1.

D. The ’357 Patent (Ex. 1002)

1. Specification

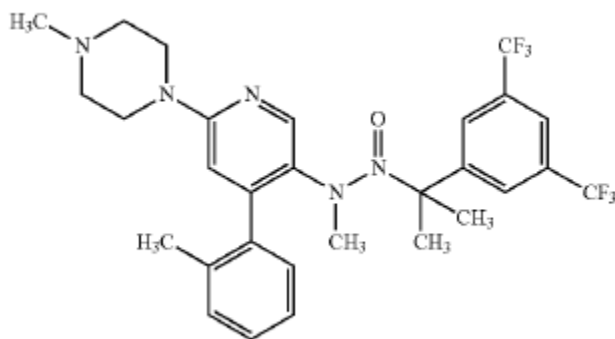
The ’357 patent is titled “Compositions and Methods for Treating Centrally Mediated Nausea and Vomiting.” Ex. 1002, code (54). The ’357 patent issued from Appl. No. 14/069,927, which claims priority back to Provisional Application No. 61/262,470 filed on November 18, 2009. *Id.* at codes (21), (22), (60), (63). As discussed below, all of the asserted prior art references pre-date the earliest possible priority date of November 18, 2009.

The ’357 patent relates to the use of centrally acting NK antagonists to treat chemotherapy-induced nausea and vomiting (CINV), and in particular treatment regimens using the combination of the 5-HT₃ antagonist palonosetron and the NK₁ antagonist netupitant. *Id.* at 1:19–25, 4:7–33. The patent also discusses the use of the corticosteroid dexamethasone as part of such a regimen. *Id.* at 1:32–36, 4:31–33.

As explained in the ’357 patent, the prior art recognized the use of 5-HT₃ antagonists, such as ondansetron and palonosetron, to control nausea and vomiting caused by various medical procedures, including chemotherapy (CINV), surgery (PONV), and radiation therapy (RINV). *Id.* at 1:28–38. The background section of the patent further notes that NK₁

antagonists recently emerged as another tool for combating nausea and vomiting from emetogenic medical procedures. *Id.* at 2:4–6. The patent indicates that the NK₁ antagonist aprepitant was approved by the Food and Drug Administration (FDA) and marketed as EMEND®, but notes that aprepitant did not show a reduction in nausea compared to other components of the anti-emetic regimen. *Id.* at 2:6–34. There was also a limited effect on nausea by another known NK₁ antagonist, casopitant. *Id.* at 2:34–49.

The '357 patent teaches that netupitant is another selective NK₁ antagonist under development by Patent Owner, with the formula 2-3,5-bis(trifluoromethyl)phenyl-N,2-dimethyl-N-4-(2-methylphenyl)-6-(4-methylpiperazin-1-yl)pyridin-3-ylpropanamide and the following structure:



Id. at 2:64–3:18. The figure above shows the chemical structure of netupitant. The patent states that, after extensive clinical testing, it was unexpectedly discovered that netupitant is active against nausea, and that a single dose of netupitant was able to treat nausea and vomiting in response to highly and moderately emetogenic chemotherapy for five consecutive days. *Id.* at 4:37–42.

Additionally, the '357 patent teaches that netupitant may be combined with other anti-emetic agents, including a 5-HT₃ antagonist such as palonosetron and a corticosteroid such as dexamethasone, to achieve

unexpectedly improved treatment outcomes. *Id.* at 4:65–67. For example, the patent explains that palonosetron is much more effective in combinations with netupitant than it is in combination with aprepitant, and that palonosetron shows an improved pharmacokinetic profile (e.g., better bioavailability) when combined with netupitant as opposed to palonosetron administered in a single dose. *Id.* at 5:2–9. The patent further explains that netupitant potentiates the effect of dexamethasone, such that dexamethasone may be administered at “sub-therapeutic doses” (i.e., doses at which dexamethasone would be ineffective if administered by itself). *Id.* at 5:13–17. In support, the patent includes data on both a complete response rate (defined as no emetic episodes, no rescue medication) and various secondary endpoints (including no emesis, no nausea, and no significant nausea) from a clinical efficacy study comparing a) netupitant (at doses of 100 mg, 200 mg, and 300 mg) combined with 0.5 mg palonosetron and a sub-therapeutic dose of dexamethasone (12 mg on Day 1) to b) 0.5 mg palonosetron combined with a standard dexamethasone dose (20 mg on Day 1) and c) aprepitant regimens combined with either ondansetron or palonosetron and dexamethasone. *Id.* at 17:1–19:45; Tables 5 and 6.

Example 4 of the '357 patent discloses administering netupitant alone to healthy human volunteers to determine occupancy of brain NK₁ receptors. The results are shown in Figure 5, reproduced below:

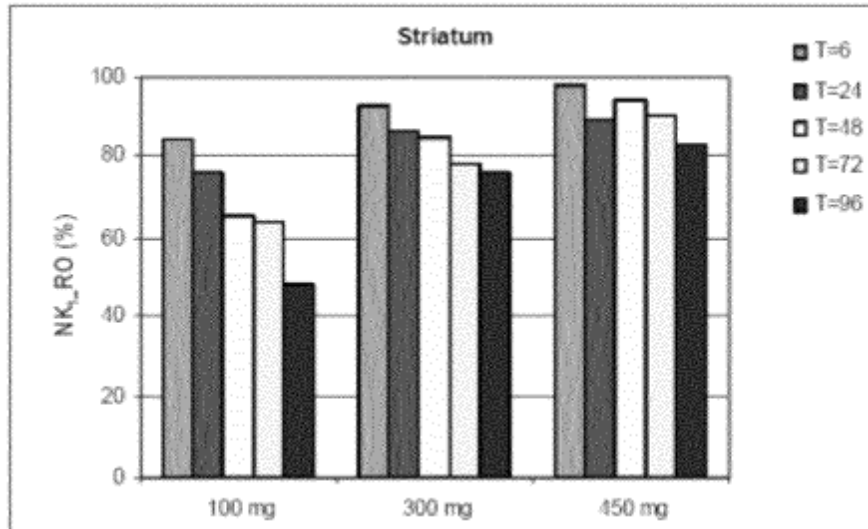


Figure 5 provides a bar graph that depicts the average NK receptor occupancy at 6, 24, 48, 72 and 96 hours after a single oral dose of 100, 300 and 450 mg. netupitant (N=2 for each dose) in striatum, as measured using positron emission topography. Ex. 1002, 6:58–62. As shown above, 90% or higher occupancy (“close to the expected C_{max} ”) of the striatum receptors was reached with half of the subjects with a single oral dose. Moreover, “[a]ll doses showed a relatively long duration of blockade of NK₁ receptors and the decline over time was dose dependent.” *Id.* at 16:37–60.

2. Illustrative Claims

Petitioner challenges claims 2–4, 11–16, 40–42, and 52–62 of the ’357 patent. Claims 2 and 4 are independent claims, and reproduced below:

2. A method of treating chemotherapy induced nausea and vomiting (CINV) in a subject receiving chemotherapy comprising administering to a subject receiving chemotherapy a regimen of netupitant and a sub-therapeutic dose of dexamethasone.
4. A method of treating chemotherapy induced nausea and vomiting (CINV) comprising inducing in a subject receiving chemotherapy blood levels of palonosetron and netupitant effective to treat said CINV.

Ex. 1002, 21:39–43, 48–51.

E. Prior Art and Asserted Grounds

Petitioner asserts that claims 2–4, 11–16, 40–42, and 52–62 would have been unpatentable based on the following grounds:

Claim(s) Challenged	35 U.S.C. §¹	Reference(s)/Basis
2–4, 11–16, 40, 52–54 and 56–62	103	Herrstedt ² , Bös ³

¹ 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).

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. 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.*

² J. Herrstedt & P. Dombernowsky, *Anti-Emetic Therapy in Cancer Chemotherapy: Current Status*, 101 Basic & Clinical Pharmacology & Toxicology 143-150 (2007) (Ex. 1010) (“Herrstedt”).

³ U.S. Patent 6,297,375 B1 (Ex. 1014) (“Bös”).

Claim(s) Challenged	35 U.S.C. § ¹	Reference(s)/Basis
41, 42	103	Herrstedt, Bös, Herrington ⁴
55	102	Herrstedt, Bös, Hargreaves ⁵

Petitioner relies on a declaration of Stephen J. Peroutka, M.D., Ph.D. (Ex. 1009) to support its Petition. Patent Owner relies on a declaration of Rudolph M. Navari, M.D., Ph.D., F.A.C.P. (Ex. 2068) to support its Preliminary Response.

II. DISCUSSION

A. *Discretionary Denial*

Patent Owner filed a request for discretionary denial of institution. Paper 8. Petitioner opposed. Paper 9. The Acting Director denied the discretionary denial request. Paper 12 (September 19, 2025). Accordingly, we proceed with our analysis of the merits of Petitioner’s patentability challenges and do not address the discretionary denial arguments presented by the parties.

B. *Level of Ordinary Skill in the Art/Expert Qualifications*

Petitioner contends that a person of ordinary skill in the art (“POSA”) relevant to the ’357 patent would be skilled in one of “clinical medicine, medical oncology, radiation oncology, oncology nursing, statistics, pharmacy, medical policy and decision making, and pharmacology.” Pet. 7 (citing Ex. 1013, 20). Petitioner further contends that such a POSA would

⁴ 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 (2008) (Ex. 1016) (“Herrington”).

⁵ 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) (“Hargreaves”).

have 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.” *Id.* at 7–8. Petitioner also asserts that its expert “Dr. Peroutka is a pharmacologist familiar with the level of skill at the critical date.” *Id.* at 8.

Patent Owner proposes the following definition for a POSA:

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

Prelim. Resp. 13 (citing Ex. 2068 ¶ 19). Patent Owner disagrees with Petitioner’s definition of a POSA to the extent it does not require experience in the field of oncology. *Id.* Patent Owner contends that Dr. Peroutka does not appear to have sufficient experience in the field of oncology to accurately opine from the perspective of a POSA as of the patent’s priority date. *Id.* at 13–14.

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. 2068 ¶¶ 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); *id.* at 11 (publication 37: article on “Neurotransmitter receptor binding studies predict antiemetic efficacy and side effects” in Cancer Treatment Reports); *id.* at 13 (publication 51: article on “Chemotherapeutic agents do not interact with neurotransmitter receptors” in Cancer Chemotherapy and Pharmacology).

C. Claim Construction

We interpret a claim “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b).” 37 C.F.R. § 42.100(b) (2019). This standard requires that we construe claims “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.” *Id.*

Petitioner proposes constructions for the phrase “inducing in a subject blood levels of palonosetron and netupitant effective to treat said CINV” recited in claim 4 and the phrase “sub-therapeutic dose of dexamethasone” recited in claim 2. Pet. 8–9. Patent Owner contends that no claim construction is necessary to resolve the parties’ disputes. Prelim Resp. 14–15. At this stage, we do not perceive a need to construe expressly any claim terms of the ’357 patent for purposes of determining whether to institute trial.

D. Overview of Asserted References⁶

1. Overview of Herrstedt (Ex. 1010)

Herrstedt is an article published in the journal *Basic & Clinical Pharmacology & Toxicology* in 2007. Ex. 1010, 143. Patent Owner does not dispute that Herrstedt is prior art to the challenged claims.

Herrstedt provides a review of antiemetic drugs used to treat nausea and vomiting caused by cancer chemotherapy, with a particular focus on two

⁶ In this section, we summarize the prior art references primarily relied upon by Petitioner and identified as the basis for the grounds set forth in the Petition. We note, however, that the record includes other relevant references reflecting the state of the art that we have considered as part of our analysis.

new classes of antiemetics: serotonin₃ (5-HT₃) and neurokinin₁ (NK₁) receptor antagonists. *Id.* It teaches that the prior combination of a 5-HT₃ antagonist and a corticosteroid improved prophylaxis of chemotherapy-induced emesis, but prophylaxis of nausea was only moderately improved with the combination. *Id.* It further teaches that adding the NK₁ antagonist aprepitant increased the effect of the combination against both “acute emesis” (occurring 0–24 hours after chemotherapy) and “delayed emesis” (occurring 24–120 hours after chemotherapy). *Id.*

With regard to corticosteroids, Herrstedt teaches that “dexamethasone is one of the most intensively investigated,” and was shown to significantly decrease acute and delayed emesis and nausea. *Id.* at 145. For patients receiving cisplatin-based, highly emetogenic chemotherapy (HEC), Herrstedt teaches that a single 20 mg dose of dexamethasone was superior, whereas a dose of 8 mg was sufficient for patients receiving moderately emetogenic chemotherapy (MEC). *Id.* Herrstedt also teaches that the combination of aprepitant and oral dexamethasone results in a two-time increase in the area under the curve (AUC) of dexamethasone, therefore indicating an inhibition of dexamethasone metabolism by aprepitant. *Id.* at 147.

With regard to 5-HT₃ receptor antagonists, Herrstedt identifies ondansetron, granisetron, tropisetron, dolasetron, and palonosetron among the available options marketed in the United States. *Id.* at 145. Herrstedt notes that “[p]alonosetron, the newest of these agents, has a very potent and specific binding at 5-HT₃ receptors and a half-life around 40 hr as compared to less than 10 hr for the other agents.” *Id.* It also teaches that ondansetron and granisetron had limited or no efficacy in delayed emesis, but

palonosetron may be the exception and was approved by the FDA for the treatment of delayed emesis from MEC. *Id.* at 145–146.

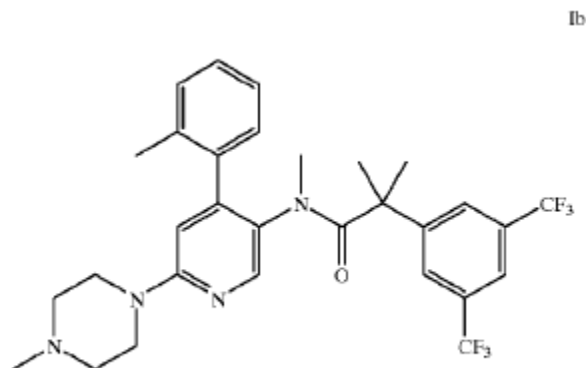
With regard to NK₁-receptor antagonists, Herrstedt indicates that only aprepitant had been marketed, and another one, casopitant, was in phase III trials at the time. *Id.* at 146. It teaches that “[d]uring the development of aprepitant, it became clear that the dose of oral (and to a minor degree intravenous) corticosteroids had to be reduced due to interaction at the cytochrome P450 (CYP) 3A4 enzyme system between corticosteroids and aprepitant.” *Id.* Herrstedt concludes that “aprepitant significantly improves the effect of ondansetron plus dexamethasone in patients receiving a combination of cyclophosphamide plus an anthracycline.” *Id.* at 147.

Herrstedt teaches that the Multinational Association of Supportive Care in Cancer (MASCC) and other organizations have issued guidelines recommending the combination of a serotonin antagonist + dexamethasone + aprepitant for prophylaxis of acute nausea and vomiting in HEC patients, and the combination of dexamethasone + aprepitant for the prophylaxis for delayed nausea and vomiting in HEC patients. *Id.* at 148–149 (Table 4). Although patients receiving an anti-emetic regimen according to these guidelines are usually protected from vomiting, Herrstedt indicates the nausea continues to be the main problem for the majority of patients. *Id.* at 148. According to Herrstedt, it is unknown if higher doses of corticosteroids might increase the effect against nausea. *Id.*

2. *Overview of Bös (Ex. 1014)*

Bös is a U.S. patent issued on October 2, 2001. Patent Owner does not dispute that Bös is prior art to the challenged claims.

Bös describes 4-phenyl-pyridine derivative compounds that function as NK₁ antagonists. Ex. 1014, Abstract. 2:1–65. Bös explains that NK₁ is the neuropeptide receptor for the naturally occurring ligand substance-P, and is involved in a number of diverse biological processes. *Id.* at 1:6–20. Among other conditions, it notes that NK₁ antagonists are useful for the treatment of motion sickness and cisplatin-induced emesis. *Id.* at 1:59–64, 4:13–20. Bös highlights compound Ib with the following structure:



Id. at 14:9–30. As shown in the figure above, compound Ib of Bös has the same chemical structure as the structure for netupitant disclosed in the '357 patent. *Cf.* Ex. 1002, 3:5–19.

Bös discloses certain in vitro and animal study results showing that compound Ib has “valuable therapeutic properties.” Ex. 1014, 14:32–34. A binding assay showed that compound Ib is a “potent and selective antagonist” for recombinant NK₁ receptors expressed in CHO cells, with a pK_i 9.0, which was over two orders of magnitude of selectivity for the NK₁ receptor compared to other binding sites. *Id.* at 18:42–48; *see also id.* at 39:48–49 (“A pK_i in the range of about 8.0 to about 9.8 indicates an especially high affinity.”). Bös also reports that compound Ib blocked emesis in ferrets and *suncus murinus*. *Id.* at 19:11–30.

3. *Overview of Hargreaves (Ex. 1012)*

Hargreaves is an article published in *The Journal of Clinical Psychiatry* in 2002. Ex. 1012. Patent Owner does not dispute that Hargreaves is prior art to the challenged claims.

Hargreaves teaches that substance P (SP)-NK₁ receptor pathways have been implicated in the pathophysiology of emesis and depression, and that clinical studies demonstrated that treatment with aprepitant (MK-0869) significantly improves depression system and reduces incidences of CINV. *Id.*, Abstract. Hargreaves also teaches that positron emission tomography (PET) studies “predicted that very high levels of central NK₁ receptor occupancy (> 90%) were associated with therapeutically significant antidepressant and antiemetic effects.” *Id.* Hargreaves establishes a relationship between plasma concentration and receptor occupancy, which showed that “high levels of NK₁ receptor occupancy were associated with significant antidepressant effects and optimal activity against CINV.” *Id.* at 23. According to Hargreaves, this analysis demonstrated that a 375 mg dose of aprepitant has no advantage over the 125 mg dose in the treatment of CINV because the same receptor occupancy level was achieved with the lower dose. *Id.*

4. *Overview of Herrington (Ex. 1016)*

Herrington is an article published in the journal *Cancer* in 2008. Ex. 1016. Patent Owner does not dispute that Herrington is prior art to the challenged claims.

Herrington describes a clinical study evaluating the combination of aprepitant, palonosetron, and dexamethasone in the prevention of acute and delayed CINV. *Id.*, Abstract. In this study, there were three different groups

(treatment arms) of patients receiving highly emetogenic chemotherapy, in which all treatment arms received a 0.25 mg intravenous dose of palonosetron on Day 1 and dexamethasone on each of Days 1–4. *Id.* The first group (Arm A) also received 125 mg oral aprepitant on Day 1 plus 80 mg oral aprepitant on Days 2–3. *Id.* The second group (Arm B) received 125 mg oral aprepitant on Day 1 but received placebo rather than aprepitant on Days 2–3. *Id.* The third group (Arm C) received placebos on Days 1–3. *Id.* The results showed that there was no significant differences between Arms A and B for emesis, nausea, or the use of break-through antiemetics, with 93% of patients in Arms A and B being emesis-free (compared with only 50% in Arm C). *Id.* This led to the conclusion that a single dose of aprepitant displayed similar effectiveness compared with 3-day aprepitant. *Id.* In considering other efficacy endpoints, Herrington notes that “[t]he incidence of overall nausea, significant nausea (>25 mm on the 100-mm visual analog scale), and the severity of nausea was not different among the 3 arms.” *Id.* at 2084, Table 4, Figure 2.

E. Rule 132 Declaration

During prosecution of the parent application, No. 13/077,462, the Examiner asserted it would have been obvious to combine netupitant, palonosetron, and dexamethasone to treat CINV because the prior art taught an aprepitant/5-HT₃ antagonist/dexamethasone combination as the “standard of care,” and further identifies netupitant as an alternative NK₁ antagonist and palonosetron as an alternative 5-HT₃ antagonist. Ex. 1005, 328. In response, Patent Owner submitted a declaration under 37 C.F.R. § 1.132 (“Rule 132 Declaration”), in which the declarants Giorgia Rossi and Claudio Pietra provided certain *in vitro* and clinical data purporting to show

unexpected results associated with the combination of palonosetron and netupitant. *Id.* at 341-350.

The Rule 132 Declaration indicates that unexpected synergy was observed from the combination with respect to the inhibition of substance-P. The declarants explained:

Because substance-P is the natural ligand for the NK-1 receptor, and palonosetron is a ligand for the 5-HT3 receptor, we did not expect palonosetron to have any effect on substance-P response. However, we unexpectedly discovered that palonosetron inhibited the substance-P response. Even more surprisingly, we discovered that other established 5-HT3 antagonists, specifically ondansetron and granisetron, did not inhibit substance-P response.

Rule 132 Decl., ¶ 12. The declaration includes the following data related to the concentration of substance-P required to induce Ca^{2+} mobilization (the “EC₅₀”):

TABLE I

Inhibition of SP response in NC108-15 cells by netupitant (netu) and palonosetron (palo).

SP + Antagonist(s)	EC ₅₀ (uM) ± S.E.M.	n
SP only	2 ± 0.2	38
Plus netu (1 nM)	2 ± 0.3	3
Plus netu (3 nM)	5 ± 3	3
Plus netu (10 nM)	10 ± 0.9	3
Plus netu (30 nM)	40 ± 10 ^a	6
Plus palo (0.2 nM)	2 ± 0.1	3
Plus palo (0.6 nM)	3 ± 0.6	3
Plus palo (2 nM)	10 ± 2	3
Plus palo (6 nM)	30 ± 6 ^a	5
Plus net (1 nM) plus palo (0.2 nM)	120 ± 20 ^b	7
Plus net (30 nM) plus palo (6 nM)	970 ± 150 ^c	5

Id. ¶ 17. As shown above, “[a]t concentrations where neither individual molecule increased the EC₅₀ of substance P, the combination of molecules increased the EC₅₀ of substance-P from 2 uM to 120 uM, a sixty-fold increase in the EC₅₀ of substance-P.” *Id.* ¶ 21. At higher concentrations,

where the additive effect of the two ingredients was expected to be 66 μ M (38 μ M for netupitant + 28 μ M for palonosetron), the declarants observed that the combination actually showed an EC₅₀ of 970 μ M, a 500-fold increase compared to substance-P only. *Id.* ¶¶ 23.

In addition, the declarants “observed an unanticipated statistically significant effect against nausea from the combination of netupitant and palonosetron that has not previously been observed in clinical studies involving the combination of aprepitant with ondansetron or aprepitant with palonosetron.” *Id.* ¶ 28. The declaration provides the following table including data from Patent Owner’s clinical trials along with certain other comparative studies (with color coding added):

TABLE 2

	1	2	3	4	4a	5	6	7	8
Efficacy Endpoint	Palo + Netu (HEC) ^a	Ondan + Aprep (HEC) ^a	Palo + Netu (MEC) ^b	Ondan + Aprep (MEC) ^c	Ondan + Aprep (HEC) ^{c1}	Palo + Aprep (HEC) ^d	Palo + Aprep (MEC) ^e	Ondan + Aprep (MEC) ^f	Palo + Aprep (HEC) ^g
Percentage of Patients with No Nausea									
Overall (0-120h)	61.5	58.2	50.3	33	48,49	nr	32 ^{ncs}	30.6	59.9 ^{ncs}
Acute (0-24h)	80.0	77.6	70.4	nr	nr,nr	nr	nr	nr	nr
Delayed (25-120h)	68.1*	60.4	53.3	nr	51,53	nr	nr	nr	nr
Percentage of Patients with No Significant Nausea									
Overall (0-120h)	89.6*	85.8	74.6*	61	73,71	88.5	56 ^{ncs}	66.1	91 ^{ncs}
Acute (0-24h)	98.5*	94.0	87.3	nr	nr,nr	nr	nr	nr	nr
Delayed (25-120h)	90.4*	88.1	76.9	nr	75,73	nr	nr	nr	nr

*Statistically Significant (p < 0.05)

nr Data Not Reported

ncs Non-Comparative Study; statistical significance not evaluated

^a Helsinn Study NETU-07-07

^b Helsinn Study NETU-08-18

^c Warr *et al.* (2005) (Ref. D)

^{c1} FDA-Approved Prescribing Information for Emend® (aprepitant) (results of two studies reported) (Ref. E)

^d Herrington *et al.* (2008) (Ref. F)

^e Grunberg *et al.* (2008) (Ref. G)

^f Yeo *et al.* (2009) (Ref. H)

^g Longo *et al.* (2012) (Ref. I)

Id. ¶ 32.

Based on the data reported above for highly emetogenic chemotherapy (HEC), the declarants indicated that “the combination of aprepitant with palonosetron was not able to produce a statistically significant reduction in nausea or significant nausea in the HEC study reported in column 5 [color coded orange], while the combination of netupitant with palonosetron reported in column 1 [color coded green] was.” *Id.* ¶ 34. With respect to moderately emetogenic chemotherapy (MEC), the declarants further concluded that “the combination of netupitant and palonosetron was able to protect 50% of the patients from nausea [shown in column 3, color coded yellow] while the combination of aprepitant with palonosetron only protected 32% of the patients [shown in column 6, color coded pink].” *Id.* ¶ 35. Likewise, “[t]he combination of netupitant with palonosetron protected 75% of the MEC patients from significant nausea while the combination of aprepitant with palonosetron only protected 56% of the patients.” *Id.* ¶ 36.

The Examiner allowed the claims in the parent application in view of the synergy and unexpected results shown in the Rule 132 Declaration. Ex. 1005, 369.⁷

F. Ground 1: Obviousness Based on Herrstedt and Bös

In Ground 1, as presented in the Petition, Petitioner asserts that claims 2–4, 11–16, 40, 52–54, and 56–62 are obvious based on the combination of

⁷ During prosecution of Application No. 14/069,927 that issued as the ’357 patent, the Examiner initially rejected the claims for obviousness-type double patenting in view of the claims allowed in the parent application, but then withdrew that rejection after a terminal disclaimer was filed. The Examiner did not cite the previously filed Rule 132 Declaration as the basis for allowance of the claims in the ’357 patent. *See* Ex. 1006.

Herrstedt and Bös. Pet. 14–38. As explained in our analysis below, we find that Petitioner has demonstrated a reasonable likelihood of prevailing as to independent claims 2 and 4 based on this ground. Our conclusion with regard to this ground is sufficient for institution based on all of the grounds identified in the Petition. *See SAS Inst., Inc. v. Iancu*, 584 U.S. 357, 370 (2018); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (interpreting the statute to require “a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition”).

1. Petitioner’s Arguments

a) Independent Claim 2

Claim 2 recites a method of treating CINV by administering a regimen of netupitant and a “sub-therapeutic” dose of dexamethasone. Ex. 1002, 21:39–43.

Petitioner relies upon Herrstedt’s teaching of prophylactically treating “[c]hemotherapy-induced **nausea and vomiting**,” which was measured using a primary endpoint of no emesis for five consecutive dates following cisplatin-based chemotherapy. Pet. 15 (emphasis by Petitioner). Petitioner cites to Herrstedt’s teaching of a triple-drug combination of a 5-HT₃ antagonist (ondasetron), an NK₁ antagonist (aprepitant), and dexamethasone. *Id.* at 16. Based on Herrstedt’s teachings, Petitioner contends that a POSA “had good reason to employ a therapeutically effective amount of an NK₁ antagonist in combination with dexamethasone.” *Id.*

Petitioner acknowledges that Herrstedt uses aprepitant, not netupitant, but contends that aprepitant was merely identified as “the first drug” in a class of selective NK₁ antagonists. *Id.* Petitioner thus turns to Bös’s disclosure of netupitant as a potent and selective NK₁ antagonist useful for

treating emesis. *Id.* at 16–17. Petitioner contends that Bös teaches a therapeutically-effective amount of its NK₁ antagonists (including netupitant) in the range of about 10 mg to 1000 mg. *Id.* at 17. According to Petitioner “Bös provides ample reason to replace Herrstedt’s NK₁ antagonist aprepitant with a therapeutically-effective amount of Bös’ new and improved NK₁ antagonist” given the suggestion in Bös that netupitant has “good CNS penetration” that would allow it to reach NK₁ receptors in the CNS to treat emesis with a reasonable expectation of success. *Id.* at 18. Petitioner cites to the animal studies described in Bös showing that netupitant “**completely blocked**” emesis. *Id.* (emphasis by Petitioner).

Regarding claim 2’s requirement of a “sub-therapeutic dose of dexamethasone,” Petitioner asserts that the ’357 patent defines the standard minimum effective dose of dexamethasone as 20 mg on day 1 and 16 mg (for HEC) or 0 mg (for MEC) on each of days 2–4. *Id.* Based on this, Petitioner contends that Herrstedt teaches administering a sub-therapeutic dose of dexamethasone as part of its triple-drug combination by disclosing a 12 mg day-1 dose of dexamethasone. *Id.* at 18–19. Petitioner additionally identifies a motivation to administer a reduced corticosteroid dose, i.e., about 25% to 50% less than the 20 mg standard dose, based on Herrstedt’s teaching that the “combination of aprepitant and oral dexamethasone results in a ***two-time increase in the AUC of dexamethasone indicating an inhibition of aprepitant on dexamethasone metabolism.***” *Id.* at 19 (emphasis by Petitioner). Petitioner contends that the experience with aprepitant would have prompted a POSA to monitor dexamethasone with netupitant because evaluating drug-drug interactions was well-known and routine in the field. *Id.* Petitioner further notes that aprepitant and

netupitant both have tertiary amines, which was a common structural feature known to inhibit CYP3A4 metabolism. *Id.* at 20–21.

b) Independent Claim 4

Claim 4 recites a method of treating CINV by inducing “blood levels of palonosetron and netupitant effective to treat said CINV.” Ex. 1001, 21:48–51.

As with independent claim 2, Petitioner relies upon Herrstedt for its teaching of an antiemetic treatment for patients receiving HEC using a 3-drug combination including a 5-HT₃ antagonist (e.g., ondansetron) and an NK₁ antagonist (aprepitant), as well as dexamethasone. Pet. 24. Petitioner further contends that Herrstedt teaches or suggests using palonosetron as its 5-HT₃ antagonist, noting that it showed beneficial properties in the treatment of delayed emesis from MEC and has an order of magnitude increase in half-life compared to ondansetron. *Id.* at 25–26. Also, for the reasons discussed with regard to independent claim 2, Petitioner contends a POSA would have been motivated to replace Herrstedt’s first-generation NK₁ antagonist (aprepitant) with Bös’s second-generation NK₁ antagonist (netupitant) due to netupitant’s excellent CNS penetration. *Id.* at 27–28. Petitioner contends that POSA would have reasonably expected success because both compounds are used for the same purpose (decreasing nausea and vomiting) through the same mechanism (NK₁ receptor antagonism, induced by therapeutically effective blood levels). *Id.* at 28. Petitioner contends that the ’357 patent does not define what constitutes therapeutically effective blood levels, but a POSA knew that administering therapeutically effective amounts of palonosetron and netupitant with dexamethasone naturally satisfies this requirement. *Id.* at 23–25.

c) *Unexpected Results*

Petitioner also preemptively addresses the alleged unexpected results associated with netupitant based on the data included in the specification and in the Rule 132 Declaration submitted during prosecution of the parent application. *Id.* at 48–60. Petitioner contends that the asserted unexpected properties for netupitant were already present for aprepitant, including efficacy for nausea. *Id.* at 48–50. Petitioner points out that the label for Emend (Ex. 1030) shows a reduction of nausea, particularly significant nausea. Pet. 50. Although statistical significance was not calculated for nausea parameters, Petitioner points out that the “complete protection” value defined as an efficacy endpoint includes a metric based on a “maximum nausea visual analogue scale [VAS] score <25 mm on a 0 to 100 mm scale.” *Id.* (citing Ex. 1030, 7). Petitioner also points out that the Emend label reports an overall improvement from 66% to 73% for significant nausea in a first study, and that a higher proportion of patients reported minimal or no impact on nausea and vomiting in a second study. *Id.* at 51. Petitioner also points out that Campos (Ex. 1023) discloses aprepitant’s therapeutic benefit for nausea during both the acute and delayed phases of CINV. *Id.* at 53.

Petitioner further contends that, despite Patent Owner’s representations, Example 5 of the patent Specification shows that aprepitant had an effect on nausea that was comparable to netupitant. *Id.* at 51–52. In arguing otherwise during prosecution, Petitioner contends that Patent Owner misleadingly excised information from Table 6’s larger data set, and that Example 5 was never designed to compare netupitant against aprepitant. *Id.* at 52. Likewise, Petitioner contends that Patent Owner’s response to the Examiner materially altered the table taken from the Rule 132 Declaration without noting the alterations. *Id.* at 54. In particular, Petitioner asserts that

the declaration excluded data from the studies purporting to show a similar effect for ondasetron + aprepitant versus palonsetron + netupitant (columns 4 and 7), instead indicating that the data was “not reported.” *Id.* at 55.

Furthermore, Petitioner points out that the data regarding aprepitant cited in the Specification’s Table 6 and in the Rule 132 Declaration came from a different study by Grunberg (Ex. 1035) with a different design, including differences in dosing, that precluded making a direct comparison to netupitant. *Id.* at 52, 56–57. Even assuming that the comparison to the aprepitant + ondansetron combination was appropriate, Petitioner points out that the data showed only marginal improvement for the highest netupitant dose and that aprepitant actually showed an improved anti-nausea effect compared to lower netupitant doses. *Id.* at 52. Petitioner contends there is no unexpected synergy between netupitant and palonosetron, nor is there a nexus between the alleged synergy and the claimed invention. *Id.* at 57–60.

2. *Patent Owner’s Arguments*

In its Preliminary Response, Patent Owner argues generally that Petitioner has not established a reasonable likelihood that any challenged claim would have been obvious. Patent Owner argues that Petitioner applies the wrong legal framework for obviousness, and relies upon impermissible hindsight, using the claims as a roadmap to cherry-pick the prior art. Prelim. Resp. 17–18. For example, Patent Owner contends that Petitioner incorrectly assumes that a POSA would first look to the aprepitant-based triple therapy used to treat CINV, which did not even allow for the treatment of nausea, and then consider swapping the then-gold-standard aprepitant for netupitant to arrive at the claimed invention. *Id.* at 18. Patent Owner contends, contrary to Petitioner’s assertions, that the obviousness question

cannot be framed to focus only on whether it would be obvious to substitute netupitant for aprepitant in Herrstedt's three-drug regimen. *Id.*

According to Patent Owner's framing, the problem facing the POSA in 2009 was the need for improved treatment of CINV that specifically controlled chemotherapy-induced nausea. *Id.* at 19. Patent Owner points out that the 2009 National Comprehensive Cancer Network ("NCCN") Guidelines indicated that lack of nausea control remained a significant problem despite reliable control of emesis using the previously known triple therapy regimen. *Id.* (citing Ex. 2037). Patent Owner contends that emesis (which includes vomiting and retching) is a separate adverse event from nausea, and that treatments for CINV did not need to demonstrate an effect on nausea to secure FDA approval. *Id.* at 5–6. Patent Owner contends that the POSA had many potential pathways to control nausea as part of a CINV treatment, including adding a fourth drug to the existing triple therapy regimen. *Id.* at 20–21. Among such options, Patent Owner identifies olanzapine, gabapentin, and cannabinoids. *Id.* at 22–23. Patent Owner contends that the failure to consider these alternate paths underscores the hindsight of Petitioner's obviousness analysis. *Id.* at 23.

Patent Owner further argues that Petitioner's assertion that netupitant was recognized as an "improved" NK₁ receptor antagonist is unsupported. *Id.* at 24. Patent Owner argues that Petitioner fails to consider other NK₁ antagonists that were known at the time. *Id.* at 24–25. Furthermore, Patent Owner argues that Bös discloses netupitant as one of millions of compounds disclosed, and there is no express language suggesting that netupitant had greater antagonist activity at the NK₁ receptor than any of those other compounds. *Id.* at 25. Patent Owner contends that Petitioner's motivation to choose netupitant, e.g., due to "good CNS penetration," is unsupported

due to the lack of any analysis comparing netupitant and aprepitant. *Id.* at 26. Patent Owner contends that “Bös’s high-level observations regarding netupitant’s antagonist activity and CNS penetration fall far short of showing the comparative efficacy of these compounds to aprepitant (or any other NK-1 receptor antagonist) for treating CINV, let alone in treating nausea.” *Id.* at 27. Patent Owner also argues that Petitioner failed to demonstrate any reasonable expectation of success in treating nausea. *Id.* at 28–29.

Patent Owner also reiterates and emphasizes the unexpected evidence results it submitted during prosecution as evidence of non-obviousness. *Id.* at 29–32. Patent Owner points to the synergy between the netupitant and palonosetron on substance P, as shown in Table 1 of the Rule 132 Declaration. *Id.* at 29–30. Patent Owner contends that this data indicates a greater clinical impact on the control of nausea, when netupitant and palonosetron are administered together, as compared to the sum of their effects when administered separately. *Id.* at 31. Patent Owner argues that Petitioner’s contention that the combination of netupitant and palonosetron had no better effect on nausea compared to other known combinations of 5-HT₃ and NK₁ receptor antagonists is not supported by any scientific evidence or data. *Id.* Patent Owner also argues that controlled clinical trials showed that aprepitant combined with 5-HT₃ antagonists (ondansetron or palonosetron) did not provide statistically significant relief for “nausea” or “significant nausea,” as compared to standard therapy, for both HEC and MEC patients. *Id.* at 32. Patent Owner further contends that it did not misrepresent any data during prosecution, and the majority of this data was readily available through the same public documents cited in the Rule 132 Declaration. *Id.* at 33, 38–39 (citing Ex. 1016, 2086 (“According to its

package insert, aprepitant fails to demonstrate improved efficacy over placebo for the prevention of nausea (overall and significant nausea) in acute [(Day 1)] or delayed phases [(Days 2-5)]” after chemotherapy). Patent Owner contends that the data from the Emend label and other industry publications, including Herrington, all confirmed there was no improved efficacy on nausea by aprepitant. *Id.* at 34–36. Moreover, with regard to the data from Patent Owner’s internal studies presented in columns 1 and 3 of Table 2 in the Rule 132 Declaration, Patent Owner states that “[i]f the Office had wanted to evaluate the underlying data, they could have simply asked Helsinn to provide it, and Helsinn would have obliged without issue.” *Id.* at 37–38.

3. *Analysis*

Based on the arguments and evidence of record at this stage, we find that Petitioner has shown a reasonable likelihood of establishing that at least claims 2 and 4 would have been obvious based on Herrstedt and Bös.

Claim 2 requires the administration of netupitant in combination with a “sub-therapeutic” dose of dexamethasone to treat CINV. As reflected in Herrstedt, the combination of an NK₁ antagonist (aprepitant) and a corticosteroid (dexamethasone) was already well-established in the prior art. Ex. 1010. Herrstedt also provides the motivation to reduce the amount of dexamethasone administered with the combination based on its teaching that the “[t]he combination of aprepitant and oral dexamethasone results in a two-time increase in the AUC of dexamethasone indicating an inhibition of aprepitant on dexamethasone.” *Id.* at 147. This reduced dexamethasone dose was administered with aprepitant in the clinical studies cited in Herrstedt. *Id.* at 146 (citing Hekseth and Poli-Bigelli studies); Ex. 1037,

4113 (Hekseth study indicating that patients received 125 mg oral aprepitant and 12 mg oral dexamethasone on day 1); Ex. 1039, 3090 (Poli-Bigelli study indicating same dosage of aprepitant and dexamethasone). As noted in the '357 patent, the minimum effective dose of dexamethasone, when used to treat CINV induced by both HEC and MEC, was recognized in the art to be 20 mg on day 1. Ex. 1002, 7:62–8:4. Accordingly, by administering only 12 mg of oral dexamethasone on day 1, the prior art studies administered a “sub-therapeutic” dose of dexamethasone with aprepitant.

Furthermore, with regard to the requirement in independent claim 4 to induce “blood levels of palonosetron and netupitant effective to treat said CINV,” Herrstedt teaches that palonosetron “has a very potent and specific binding at 5-HT₃ receptors” with a half-life around 40 hours (compared to less than 10 hours for other agents), which also exhibited improved treatment of delayed emesis compared to ondansetron and granisetron. Ex. 1010, 145–146. We find that these properties would have motivated a POSA to choose palonosetron over other types of 5-HT₃ antagonists for the treatment of emesis. Given the significant half-life of palonosetron, and its administration via the circulatory system, we also find that the administration of palonosetron at the clinical doses taught by Herrstedt would satisfy the claim requirement of inducing “blood levels” effective to treat CINV.

Herrstedt taught the use of aprepitant as an NK₁ receptor antagonist that could be combined with dexamethasone and/or palonosetron to treat emesis. Nonetheless, based on Bös’s identification of netupitant (compound Ib) as a “potent and selective” NK₁ antagonist with “valuable therapeutic properties,” the present record supports Petitioner’s argument that the POSA would have been motivated to replace aprepitant with netupitant in the

combination therapy. Ex. 1014, 14:31–34. Bös indicates that the compounds disclosed therein have utility in the treatment of emesis, and that netupitant in particular “is a potent antagonist of NK₁ induced behaviors in Gerbil and blocks emesis in Ferrets and suncus murinus with similar potency.” *Id.* at 19:26–30. Bös further indicates that netupitant has a high affinity for the NK₁ receptor and a prolonged half-life. *Id.* at 18:44–48, 19:31–38. In view of these properties, we find a POSA would have had good reason to consider netupitant as a potential replacement for aprepitant in the treatment of CINV. Bös also teaches that the daily dosage can be adjusted between 10 to 1000 mg per person, or above that upper limit when necessary, and that the effective amount can be fitted to the individual requirements in each particular case. *Id.* at 42:5–11. As with palonosetron, given the significant half-life of netupitant, and its administration via the circulatory system, we find that a POSA would also have been motivated to adjust the dose of netupitant to an amount that induces “blood levels” effective to treat CINV.

We have considered, but are not persuaded by, Patent Owner’s arguments to the contrary at this stage. We find unavailing Patent Owner’s contention that a POSA would not have had a sufficient reason to select netupitant among millions of other compounds disclosed in Bös. Compound Ib is extensively highlighted in Bös among other NK₁ antagonists, and was the subject of both *in vitro* testing and animal studies showing potential utility in the treatment of emesis. Ex. 1010, 14:9–19:30. To be sure, Bös does not include any comparative analysis between netupitant and aprepitant, nor does it include data assessing netupitant’s potential efficacy in controlling nausea. Such data, however, is not necessary to provide the requisite reason to combine. Although the inventors purport to have

discovered that netupitant shows improved control of nausea compared to aprepitant, “neither the particular motivation nor the avowed purpose of the patentee controls” for purposes of obviousness. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 419 (2007). Rather, “[w]hat matters is the objective reach of the claim.” *Id.*

Here, regardless of whether a POSA would have known about netupitant’s improved anti-nausea properties, we find that Bös’s identification of the compound as a “potent and selective” NK₁ antagonist with “valuable therapeutic properties” is more than sufficient for the POSA to pursue it as an alternative to aprepitant for the treatment of CINV. *Id.* at 421 (“[A] person of ordinary skill has good reason to pursue the known options within his or her technical grasp.”). Given the favorable pharmacokinetic properties reported in Bös for netupitant, and its similar mechanism of action to aprepitant (NK₁ receptor antagonism), we further find that a POSA would have had a reasonable expectation of success in replacing aprepitant with netupitant for the same therapeutic indication. *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.”).

Finally, we have considered the alleged unexpected results evidence, but do not find that it forms a sufficient basis to negate Petitioner’s reasonable likelihood of prevailing based on the present record. With regard to the alleged synergistic effect of the netupitant + palonosetron combination on substance P inhibition shown in Table 1 of the Rule 132 Declaration, there is no comparison made to the combination of aprepitant + palonosetron

taught in Herrstedt. As such, that data does not demonstrate any unexpected results compared to the closest prior art teaching. *See Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014)

(“[E]vidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art.”).

Furthermore, while Table 2 of the Rule 132 Declaration does include comparisons to the palonosetron + aprepitant combination, those comparative results were obtained from different studies (by Grunberg and Longo), and it is not clear that the criteria used in those studies were the same criteria used in Patent Owner’s clinical studies administering the combination of palonosetron + netupitant. Moreover, contrary to Patent Owner’s contention that the prior art did not recognize anti-nausea properties for aprepitant, Campos demonstrated reduced nausea scores for the combination of aprepitant (MK-869) + granisetron + dexamethasone. Ex. 1023, 1763–1764. As such, it is not clear that a reduction in nausea could be considered an unexpected property unique to netupitant.

III.CONCLUSION

For the forgoing reasons, Petitioner has demonstrated a reasonable likelihood that at least one challenged claim of the ’357 patent would have been unpatentable over the prior art of record. Accordingly, we institute an *inter partes* review on all claims and all grounds set forth in the Petition.

IV.ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314, an *inter partes* review is instituted on all challenged claims and grounds set forth in the Petition;

and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, *inter partes* review of the '357 patent shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

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Patent 9,186,357 B2

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