UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HOPEWELL PHARMA VENTURES, INC.,
Petitioner

v.

MERCK SERONO S.A.,
Patent Owner

Case IPR2023-00480
U.S. Patent No. 7,713,947

PETITIONER'S REPLY TO PATENT OWNER RESPONSE

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1001	De Luca, G., et al., "Cladribine Regimen for Treating Multiple Sclerosis," U.S. Patent No. 7,713,947 B2 (filed June 18, 2007; issued May 11, 2010)
1002	Declaration of Aaron Miller, M.D.
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1004	File History for U.S. Patent No. 7,713,947
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1051	U.S. Patent and Trademark Office, Memorandum, Interim Procedure for Discretionary Denials in AIA Post-Grant Proceedings with Parallel District Court Litigation (June 21, 2022)
1052	Supplemental Declaration of Aaron Miller, M.D. (*served not filed*)
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1059	Transcript of the Deposition of Nicholas S. Bodor. Ph.D. (CONFIDENTIAL – PROTECTIVE ORDER MATERIAL)
1060	Transcript of the Deposition of Yogesh Dandiker, Ph.D. (CONFIDENTIAL – PROTECTIVE ORDER MATERIAL)
1061	Transcript of the Deposition of Fred D. Lublin, M.D.
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I. INTRODUCTION

Merck emphasizes "weight-based-dosing," arguing "the dose each patient receives is based on that individual's weight." POR, 19-24, 34-37, 48-49. But the Board already rejected Merck's narrow claim interpretation—finding no requirement for "active, *a priori*, steps"—and Merck offers no reason to accept its arguments now. Decision, 35-36, fn17. The claims encompass both flat and weight-based regimens. EX1084, ¶¶31–32.

Under *Duncan Parking*, Merck fails to disqualify Bodor. Addressing only Bodor's ***regimen,*** Merck ignores other relevant disclosures and Bodor and Dandiker's contributions to Bodor's tablets. Still, Merck suffers a failure of proof and lacks corroboration; no evidence links Serono's work to Bodor's disclosure. Arguing Bodor's regimen is flat-dosing, Merck offers only weight-based-dosing "corroboration," which Merck asserts is "fundamentally different." Merck can't have it both ways.

Merck asserts POSAs doubted cladribine's benefits and safety. POR, 1, 5-6. But, the patent's "Background" acknowledges art suggesting cladribine is "useful" for MS. EX1001, 2:24-3:21; Decision, 4. So did Bodor, Stelmasiak, Beutler, Romine, Sipe, Selby, and Rice. Focusing solely (and erroneously) on EDSS, Merck disregards art demonstrating cladribine safely reduced relapses and brain lesions, though no particular metric or degree of efficacy is required. Pet., 19–22;

EX1013, 4, 7; EX1031; EX1061, 136:3-8; EX1084, ¶94.

Futilely, Merck myopically focuses on Bodor's bioavailability, ignoring other indisputably desirable features: higher absorption, lower interpatient variability, convenience, lower cost, and higher stability. POR, 49-53, 55-57; Pet., 22-23; EX1002, ¶58; EX1084, ¶¶58-59. Merck disparages Bodor's bioavailability although it was at least comparable to Stelmasiak's (35.7-52.1% versus 37-51%), making Bodor's tablets "successful." EX1059, 38:18-40:17; EX1080, ¶¶16, 34, 63, 78; EX1084, ¶60. Regardless, Bodor's tablets need not be "preferred" or "most desirable."

Without support, Merck wrongly posits routine-optimization must correlate with ***therapeutic efficacy***, but the doctrine applies to ***any*** property known to be affected by the optimized variable. As Lublin concedes, POSAs routinely counted lymphocytes to avoid immune-system oversuppression. Pet., 15–17; EX1002, ¶95, 104; EX2051, ¶74; EX1061, 72:8–13; EX1084, ¶¶87.

Alleged secondary considerations lack nexus and are of no avail, e.g., Merck fails to show unexpected results over the closest prior art.

II. BODOR IS "BY ANOTHER"

A. Hopewell Met its Burden.

Bodor is prior art because nothing in Bodor facially "represent[s] the work of a common inventive entity." *EmeraChem Holdings v. Volkswagen*, 859 F.3d

1341, 1345 (Fed. Cir. 2017). Bodor lists Bodor and Dandiker as "Inventors." EX1022, (71), (75). The patent lists De Luca, Ythier, Munafo, and Lopez-Bresnahan as inventors (collectively "Serono"). EX1001, (75).

Patent No.: US 7,713,947 B2	**(10) International Publication Number WO 2004/087101 A2**
(75) Inventors: **Giampiero De Luca**, Conches/Geneva (CH); **Arnaud Ythier**, Collex-Bossy (CH); **Alain Munafo**, Tartegnin (CH); **Maria Lopez-Bresnahan**, Lincoln, MA (US)	(71) **Applicant** *(for all designated States except US)*: **IVAX CORPORATION** [US/US]; 4400 Biscayne Boulevard, Miami, Florida 33137 (US).
(73) Assignee: **Merck Serono S.A.**, Coinsins, Vaud (CH)	(72) **Inventors; and** (75) **Inventors/Applicants** *(for US only)*: **BODOR, Nicholas, S.** [US/US]; 10101 Collins Avenue, #4A, Bal Harbour, Florida 33154 (US). **DANDIKER, Yogesh** [GB/GB]; 17 New Road, Digswell, Welwyn Garden City Herts AL6 OAE (GB).

Neither the patent nor its file history evince a joint research agreement. 35 U.S.C. § 103(c)(2)(C). Hopewell met its burden.

B. Merck Fails to Meet its Burden

The burden of production shifted to Merck to show Bodor was *not* "by another." *Dr. Reddy's v. Horizon*, IPR2018-00272, Paper 74, at 14-19 (P.T.A.B. Sept. 9, 2019) (shifting burden to Patentee to provide evidence the reference is not prior art). Merck fails.

***Duncan* step 1** requires that Merck identify which portions of Bodor were "relied upon *and* relevant to establishing obviousness." *Google v. IPA Techs.*, 34 F.4th 1081, 1086 (Fed. Cir. 2022). Merck asserts Hopewell relies only upon "6 lines of Bodor" (23:15-20) disclosing a dosing regimen (the "6-line disclosure"). POR, 12. But Merck is wrong—Hopewell relies on additional Bodor disclosures

relevant to obviousness:

Relied-Upon Disclosures	EX1022	Petition
Benefits of oral cladribine	2	3
MS treatment at dosages achieving therapeutic results	22:17-19	41
Fine-tuning cladribine's dose/length	24:1-9	41-42
Cladribine tablets for treating MS	Examples 1-4	33, 43-45

EX1002, ¶¶91-119. Merck ignores relied-upon disclosures, and doesn't refute their relevance to obviousness, failing *Duncan* step 1.

***Duncan* step 2** requires showing Serono alone conceived Bodor's relied-upon disclosure. Ignoring the disclosures tabulated above, Merck fails again.

Additionally, Merck ignores Bodor and Dandiker's contributions to Bodor's disclosed tablets and regimen. By characterizing Bodor's disclosure as only a "regimen" (POR, 13), Merck misapprehends the importance of the dosage form.

Bodor:

> into a solid oral dosage form. At the present time, it is envisioned that, for the treatment of multiple sclerosis, 10 mg of cladribine in the instant complex cladribine-cyclodextrin complex in the instant solid dosage form would be administered once per day for a period of five to seven days in the first month, repeated for another period of five to seven days in the second month, followed by ten months of no treatment. Alternatively the patient

EX1022, 23:15-20 (annotated).

Bodor and Dandiker swore they invented Bodor's "instant solid dosage form." EX1059, 25:13-26:2, 111:18-119:12; EX1060, 87:15-89:2, 108:18-119:8;

EX2054, ¶16; EX2055, ¶13; EX1057, 159-160; EX1058, 9-10. Bodor establishes its tablets were "especially suited" for oral regimens. Pet., 45-47. And, Munafo admits Bodor's tablets "became an element that we were considering when designing this dosing regimen." EX1063, 62:19-63:7, 79:8-80:4.

Bodor and Dandiker recognized the tablets' importance to MS treatments, as they are the sole inventors of MS treatment methods using those tablets, claimed in USPNs 7,888,328 and 8,785,415 (priority to Bodor). EX1022, claims 25, 27-28; EX2029, claims 54, 56, 61, 75; EX2069, claims 35, 37. Furthermore, Bodor and Dandiker testified their tablets exhibited properties critical in Bodor's regimen: increased absorption, bioavailability, "reduced interpatient variation," increased patient "convenience." EX1059, 34:11-40:8, 41:5-44:8; 59:9-60:14; EX1060, 48:15-49:13, 120:2-9, 121:21-123:7, 124:11-125:6; EX1062, 42:1-47:16, 48:7-57:21. The tablets are also integral to the additional relied-upon disclosures for Hopewell's arguments. EX1022, 1-2, 22:17-19, 24:1-9, Examples 1-4; Pet., 33-45.

Because Bodor and Dandiker invented, and had kept confidential, the tablets underlying ***all*** relied-upon disclosures, Merck cannot establish invention by Serono alone. *Google*, 34 F.4th at 1084 (the difference of a single inventor constituted a different inventive entity); EX1059, 93:14-94:5; EX1060, 97:16-98:18.

Munafo's testimony cannot satisfy Merck's burden; corroboration is required. *EmeraChem*, 859 F.3d at 1346 (finding an inventor's testimony, standing

alone, insufficient). Munafo generically testified Serono designed the regimen, but he could not identify anyone's specific intellectual contribution. EX1063, 89:17-90:6; 92:17-93:13, 94:4-95:8. Moreover:

- De Luca's name appears nowhere in EX2049-2050. EX2053, ¶21; EX2049; EX2050. Merck failed to carry its burden to demonstrate De Luca made an inventive contribution.
- Neither EX2049 nor EX2050 identifies who suggested to create a 10 mg tablet—Munafo testified "it was a joint team agreement." EX1063, 135:9-14, 64:22-65:10.
- While Bodor's regimen involves administering cladribine for "***five to seven***" [1] days, Merck's documents disclose only ***five*** days. EX2050, 4-5; EX2049, 47-51; EX2053, ¶¶37-38, 41-46; EX1022, 23:15-20. Munafo's assertion that "we at Serono" considered "6 or 7 days per month" stands uncorroborated. EX2053, ¶¶47-48; *EmeraChem*, 859 F.3d at 1346. Moreover, the '247 Provisional shows that ***Dr. Bodor*** invented this seven-day frequency. EX2046, 20:6-10; POR, 17; EX2054, ¶25; EX2055, ¶22. As Munafo admitted, the "[f]requency of administration" is "an integral part of" a regimen; Merck has not shown Serono invented it. EX1063, 63:17-64:14.

[1] Unless noted, bold, italicized text reflects added emphasis.

Furthermore, Munafo concedes EX2050 and EX2049 disclose only weight-based regimens, while Bodor's regimen is flat. POR, 12-13, 17; EX1063, 119:14-121:2, 141:2-142:13, 146:9-147:6, 153:3-14, 168:2-169:1; EX2049, 47-49; EX2050, 4; EX1022, 23:15-20; EX2046, 20:6-10. Merck cannot corroborate testimony by using weight-based regimens, which Merck alleges is "fundamentally different"[2] from flat regimens. POR, 19-24.

EX2049-2050 undermine the assertion Serono conceived Bodor's regimen because both show other, unaccounted-for employees involved with cladribine. EX2050, 1; EX2049, 1; EX1063, 7:20-8:2, 81:16-86:16, 97:12-99:13.

[redacted]

[2] Hopewell does not concede weight-based and flat dosing are fundamentally different.

EX2050, 1:

Serono Participants:
I. Emery, G. Francis, D. Frank, M. Lopez-Bresnahan, A. Munafo, A. Ythier, A. Jaber, by phone: N. Ammoury, J. Hillier
IVAX Participants:
S. Marcus, Y. Dandiker, D. Weiner, by phone: D. Emma

Bodor and Dandiker's unawareness of anyone at IVAX developing the regimen does not prove Bodor's regimen came from Serono. EX2054, ¶28; EX2055, ¶25; EX2053, ¶¶50-54.

Bodor and Dandiker were unable to recall basic details of IVAX's cladribine team—names, roles, or numbers—because "it was 20 years ago." EX1059, 92:11-94:4, 100:4-21; EX1060, 49:15-50:1, 65:10-69:8. IVAX had approximately 10,000 employees world-wide at the time; others could have developed the regimen. EX1055, 13, 19; EX1056, 13, 21; EX1059, 68:12-70:12, 71:1-73:3, 81:3-86:17. Bodor's '247 provisional demonstrates Bodor's drafter was knowledgeable of cladribine regimens. EX2046, 20:6-10; EX1022, 25:24-29.

Merck relies on sheer speculation that it was "highly likely" Bodor's regimen came from Serono. EX2054, ¶28; EX2055, ¶25. Neither Bodor nor Dandiker has presented facts sufficient to corroborate such long-past events. *Price v. Symsek*, 988 F.2d 1187, 1195 (Fed. Cir. 1993).

Bodor admits never communicating with ***anyone*** from Serono, and, until deposed, had never heard of any Serono inventors. EX1059, 31:9-10, 125:22-

128:5, 129:18-130:11, 133:22-134:3. Dandiker admits not knowing what regimen (if any) Serono might have communicated to him, or whether Serono ever communicated any regimen to IVAX. EX1060, 119:13-120:16, 123:9-21, 213:1-214:18, 215:6-217:10. Bodor and Dandiker met only once and did not discuss regimens. EX1059, 89:5-20, 90:1-92:22, 104:17-105:21. Unlike *In re Mathews*, Bodor and Dandiker cannot corroborate Serono invented Bodor's disclosures or communicated them to Bodor's drafter. POR, 11-12; 408 F.2d 1393, 1394-95 (C.C.P.A. 1969). Similarly, Munafo never communicated with IVAX's legal team. EX1063, 114:21-115:20.

Bodor cites two provisionals bearing IVAX attorney docket numbers, both entitled "Cladribine ***Regimen*** for Treating Multiple Sclerosis."

EX1022, 25:24-29 (annotated):

> months of no treatment. For further dosing information, see also U.S. Provisional Patent Application No. _____ [IVAX0021-P-USA/Attorney Docket No. 033935-011], and U.S. Provisional Patent Application No. _____ [IVAX0022-P-USA/Attorney Docket No. 033935-012], both entitled "Cladribine Regimen for Treating Multiple Sclerosis", both filed on March 25, 2004 and incorporated by reference herein in their entireties.

Bodor's drafter, whom no one could identify, had access to cladribine regimens and plausibly contributed to the relied-upon disclosures. EX1022, 25:24-29; EX2053, ¶9; EX2054, ¶22; EX2055, ¶20; EX1059, 124:22-125:17; EX1060,

91:21-93:12; EX1063, 147:7-149:4. Merck produced no testimony from Bodor's drafter.

Regarding *Duncan* step 3, Bodor and Dandiker's invention of their tablets (§II.B.2.a) is "significant enough" to render them at least co-inventors of ***all*** relied-upon disclosures. Their testimony denying inventing the regimen should be given no weight because they did not understand the requirements for inventorship. EX2054, ¶26; EX2055, ¶23; EX1059, 106:3-108:9; EX1060, 211:5-13. Moreover, Bodor and Dandiker only addressed the disclosed ***regimen***, not all relied-upon disclosures. Merck fails step 3.

Were the burden to shift back to Hopewell, Hopewell nonetheless established that Bodor is prior art because Bodor and Dandiker's tablets render them co-inventors of all relied-upon disclosures.

III. CLAIM CONSTRUCTION

The Board's construction encompasses Hopewell's construction; Hopewell's arguments apply under either. Pet., 29-33; Decision, 17.

As Lublin concedes, the claims are not limited to any efficacy degree or metric. EX1001, 19:14-16; EX1084, ¶¶18, 29; EX1061, 136:3-8. Yet Merck's obviousness rebuttals wrongly focus on EDSS, disregarding other efficacy metrics. POR, 7, 33, 38–39, 50–51, 53–55, 56, 58, 61–62. Consistent with clinical practice, the patent considers relapse rate and brain lesions as efficacy metrics. EX1001,

5:52-63; EX1084, ¶¶18, 22, 24, 28, 30; EX1061, 41:18-22, 44:4-14.

Claim 39's total induction and maintenance doses are "about 1.7 mg/kg," connoting a range above and below 1.7. EX1001, 20:5-7. EX1084, ¶¶33-35. During prosecution, Merck distinguished art based on the claims requiring a ***lower*** maintenance dose than induction. EX1004, 251. Merck similarly distinguished related USPN 8,377,903's claims from the art, though it expressly claimed "about 1.7 mg/kg" for both doses. EX1025, 151. Merck limited the claims— including claim 39—to a maintenance dose ***lower*** than the induction dose. EX1084, ¶¶27, 33-35; *Andersen v. Fiber Composites*, 474 F.3d 1361, 1374 (Fed. Cir. 2007) (argument distinguishing art is a claim-scope disclaimer). This construction applies despite, e.g., claim 1 specifying a maintenance dose lower than the induction dose, because "surplusage may exist in some claims," where necessary to reflect the patentee's disclaimer. *ERBE v. Canady*, 629 F.3d 1278, 1286-87 (Fed. Cir. 2010).

IV. MERCK'S ERRORS PERVADE ITS ARGUMENTS.

A. Merck's weight-based dosing arguments improperly limit the claims.

Merck relies on "weight-based dosing" arguments, contending Bodor and Stelmasiak disclose "flat," not "weight-based," dosing (arguing no motivation "to modify Bodor's ***flat*** cladribine dosing … to arrive at the claimed ***weight-based*** dosing."). POR, 19-24, 34-37, 48-49, 52 (emphasis in original); EX1061, 145:4-8; EX2051, ¶164-166; EX1084, ¶¶10, 31-32, 62-68. But Merck's arguments should

be rejected as weight-based dosing is not a claim element.

Merck asserts, in "weight-based dosing," "the dose each patient receives is ***based*** on that individual's weight." POR, 19, 36; EX2051, ¶¶85-94; EX2052, ¶¶66-69. That is, the dose a patient receives is calculated *a priori* based on weight. EX1084, ¶31. Merck does not identify any term justifying limiting the claims to weight-based dosing. Merck and Lublin improperly import "weight-based" into the claims. POR, 19-24, 34-37, 48-49, 52; EX1061, 145:4-8.

Merely reciting "mg/kg" does not transform the claims into weight-based-dosing claims. EX1084, ¶¶31-32, 62-68. It simply requires "reaching" a certain mg/kg "at the end of the [] period." *Id.*; EX1001, 19:14-31. Though the claims ***encompass*** weight-based (and flat) dosing, they are not limited to one. EX1084, ¶32.

The Board already correctly rejected Merck's weight-based dosing arguments, concluding the claims do ***not*** require "any active, *a priori*, steps of determining an individual patient's weight and performing calculations to arrive at a mg/kg dosing before any drug is administered." Decision, 31-32, 34-38, 42-44, fn17. The Board recognized: The claims "passively recite[]" the dose "*reached at* the end." *Id.* (emphasis in original). Merck provides no reasons to conclude otherwise.

To support its flawed arguments, Merck mischaracterizes Miller's dose

calculation for average-weight patients as "impermissible hindsight," allegedly inconsistent with Miller's pre-IPR video calling MAVENCLAD's regimen "rather unique" as "the dose [was] determined by how much the individual weight is." POR, 21-22; EX1084, ¶67; EX2008, 4:17-5:1. But his statement was based on ***approved*** MS drugs, as is evident, e.g., from the video highlighting MAVENCLAD as a "new medicine" "approved" for MS. EX2008, 2:1-8; EX1084, ¶67. Miller's statement was not an obviousness opinion from POSAs' perspective considering all pertinent art. *Id.* Merck wrongly equates "unique" with non-obviousness; at most, "unique" connotes novelty. Miller's MAVENCLAD statement is not coextensive with the claims, which encompass obvious regimens. EX1084, ¶67.

B. Prior art demonstrates cladribine's efficacy and safety.

Merck wrongly argues, POSAs were "skeptical about cladribine's utility" due to "lack of cladribine clinical efficacy" and "safety concerns." POR, 5-6, 25-27, 31-32, 54-55. As the Board correctly determined, the prior art demonstrated cladribine's efficacy and safety in treating MS. EX1084, ¶¶7, 17-18, 51-57, 74-75, 77; Decision, 49-50.

1. Merck ignores art showing efficacy.

Prior-art studies demonstrate cladribine reduces relapses and/or brain lesions, which Lublin does not dispute. EX1084, ¶¶7, 16, 18, 51, 52, 93, 94;

EX1013, 7; EX1031, Abstract, 38-39; EX1018, Abstract, 1153; EX1016, 420; EX1014, 1718-19; EX1061, 41:18-19, 62:4-5. E.g., Stelmasiak reports a "very marked" relapse reduction. EX1013, 7; EX1084, ¶51. Romine reports "a statistically significant favorable effect … on the … severity of relapses" and "complete[] suppress[ion]" of lesions. EX1031, Abstract; EX1084, ¶51. The patent itself acknowledges prior art suggesting cladribine for treating MS. EX1001, 2:24-3:21; EX1084, ¶¶30, 93.

Although Lublin concedes EDSS is "challeng[ing]," "subjective," "not linear," and the doctors "don't use … mean EDSS any more," Merck improperly focuses only on EDSS in assessing efficacy. EX1061, 40:16-41:7, 48:11-15, 49:10-50:12; POR, 5-7, 54; EX1084, ¶¶23, 53. The claims do not require any particular degree or metric of efficacy and encompass relapse rate, EDSS, and brain-lesions metrics. *Section* III.A; EX1084, ¶¶28-30. POSAs would not have ignored these metrics, and a single metric is sufficient to show efficacy. EX1084, ¶¶18, 54, 111; EX1061, 52:11-15.

As Lublin concedes, even Stelmasiak's EDSS data (showing reduction during induction, cladribine-free, and maintenance periods, followed by return to baseline) was positive, indicating that MS ***did not worsen***. EX1084, ¶¶52, 94-95; EX1061, 57:3-4; EX1002, ¶¶41, 90, 101. And, efficacy need not be permanent. EX1084, ¶¶52, 70, 94-95.

Merck misrepresents Miller's 2000 statements (EX2005) as skepticism, but those statements were not offered from POSAs' perspective considering all art. EX1084, ¶103. Merck's other skepticism arguments also fail (*Section* VIII). EX1084, ¶¶101-117.

2. Merck ignores art showing safety.

Merck wrongly argues against retreatment due to allegedly "significant long-term safety concerns." POR, 5-6, 25-27, 31-32. However, the art reported that cladribine was safe. EX1084, ¶¶7, 12, 55-57, 74-78, 114; EX1013, 7; EX1047, Abstract; EX1031, 41; EX1018, 1153. Stelmasiak reported no "clinically significant hematological side effects," only "mild" side effects. EX1013, 7; EX1084, ¶¶56-57, 75, 77, 131. Romine reported "no side effects." EX1031, 41, 43; EX1084, ¶¶56-57. Moreover, POSAs would have understood Romine's statements about "long-term toxicity" to be unrelated to cladribine in view of Romine's (and Stelmasiak's) data and conclusions. EX1084, ¶57. No safety concerns discouraged using cladribine for MS, which POSAs continued to do. EX1084, ¶¶55-57, 74-78; Pet., 19-22; EX1002, ¶95, 103. Merck distorts Miller's testimony arguing he ignored cladribine's safety concerns; but Miller *expressly* considered these aspects while forming his opinions. EX1002, ¶¶50, 91, 95, 102-103; EX1084, ¶¶69, 87-88; POR, 26.

C. Bodor's bioavailability is not lower than Stelmasiak's.

Merck alleges Stelmasiak's oral solution has "higher bioavailability" than Bodor's tablets. POR, 49-52, 55-57. Not so. Merck ***understates*** Bodor's bioavailability and ***overstates*** Stelmasiak's. They were at least comparable. EX1080, ¶¶27-77, 66-73; EX1084, ¶¶8, 15, 60, 91, 94.

Merck focuses on the bioavailability in Bodor's Table VIII (39.1%), but ignores Table VI disclosing 35.7%-52.1% bioavailability. EX1080, ¶¶18, 54, 62, 68, 72-73, 79; EX1084, ¶¶15, 60; EX1022, Tables VI, VIII (annotated with red boxes below).

TABLE VIII

Ratios of Oral to I.V. Pharmacokinetic Parameters and Corresponding Lower Limit (LL) for the one-sided 95% Confidence Interval for Cladribine Study (n=26)

Pharmacokinetic Parameter	Oral Administration			
	3.0 mg		10.0 mg	
	Ratio*	LL	Ratio*	LL
AUC_{inf}	34.5	31.7	39.1	35.9
AUC_t	34.0	31.2	39.4	36.1

*Ratios (dose normalized) and Corresponding 95% LL obtained via inverse transformation of log-transformed data.

***

TABLE VI

Ratios of Oral to Subcutaneous Pharmacokinetic Parameters and Corresponding Two-Sided 90% Confidence Intervals for Cladribine Study (n=12).

Pharmacokinetic Parameter	3 mg Tablet 1		3mg Tablet 2		3mg Capsule	
	Ratio*	LL, UL	Ratio*	LL, UL	Ratio*	LL, UL
AUC_{inf}	43.1	35.7, 52.1	38.4	31.8, 46.4	38.9	32.1, 47.0
AUC_t	41.9	34.6, 50.8	37.2	30.7, 45.0	37.6	31.0, 45.5

*Ratios (dose normalized) and Corresponding 95% LL obtained via inverse transformation of log-transformed data.

Stelmasiak does not measure bioavailability. Decision, 45; EX2052, ¶¶56, 83; EX1080, ¶¶50, 57, 69, 71; EX1084, ¶¶15, 60. Instead, Stelmasiak refers to Liliemark 1992's "approximately 50%" bioavailability.[3] EX1013, 5; EX2043, Abstract, 1516, Table 1; EX1080, ¶¶69, 70; EX1084, ¶60. Merck cites Liliemark 1992 but ignores later-published Liliemark 1997 reporting 37-51% bioavailability for oral solutions:

Petition's Reference	**Bioavailability**
Stelmasiak (citing Liliemark 1992)	48, 55% ("approximately 50%")
Liliemark 1997	37-51%

[3] A lack of washout periods overinflated Liliemark 1992's bioavailability; Bodor's regimen included cladribine-free periods, avoiding such concerns. EX1074, 982; EX1022, (Examples 4, 5); EX1080, ¶71.

EX1080, ¶69; EX1013, 5; EX2043, Abstract, 1516, Table 1; EX1048, 3 EX1084, ¶60.

Liliemark 1997's reported 37-51% bioavailability was supported by general knowledge in the art, rebutting Merck's arguments:

Prior Art	Bioavailability
Liliemark 1992	48, 55% ("approximately 50%")
Albertioni	42, 46%
Saven	37%

Id., ¶67; EX2043, Abstract, 1516, Table 1; EX1064, Abstract, Table 2; EX1074, Abstract, Table 3.

Comparing Bodor's bioavailability (35.7-52.1%) with Liliemark 1997's (37-51%) refutes Merck's contention that Stelmasiak's/Liliemark's oral solution has higher bioavailability than Bodor's tablets. EX1080, ¶¶18, 73, 76; EX1084, ¶¶15, 60.

V. THE ART DISCLOSES ALL ELEMENTS OF CLAIM 36.

Merck's weight-based arguments should be rejected (*Section* IV.A). Merck's remaining arguments also fail (EX1084, ¶¶1-133):

A. The prior art teaches the claimed dosing.

Merck distorts Hopewell's position and the art. POR, 19-23, 36. As Lublin concedes, the claims neither require nor exclude treating any particular-weight

patients. EX1061, 135:1-10; EX1084, ¶¶31-32. Merck cannot credibly contend that POSAs lack the common sense and ordinary creativity to treat average-weight patients (70 kg/154 pounds). Pet., 48-51; EX1084, ¶62. The art supports applying Bodor's dosing to average-weight patients: e.g., Stelmasiak treated 52-75 kg patients, without excluding patients of any weight. EX1013, 5; EX1084, ¶¶65-66. Further, Hopewell was not required show administering "every" dose to an average-weight patient, because the claims don't require it. *Janssen Pharma. v. Teva Pharma*., Nos. 2022-1258, 2022-1307, at 17 (Fed. Cir. Apr. 1, 2024).

Curiously, Merck argues Hopewell did not show Stelmasiak discloses the claimed induction dose. But Hopewell relied on Bodor's dosing—not Stelmasiak's. Merck alleges Stelmasiak teaches away, but Merck fails to show that the art or Stelmasiak "criticize[d], discredit[ed], or otherwise discourage[d]" the claims. *Allergan v. Sandoz*, 796 F.3d 1293, 1306 (Fed. Cir. 2015); POR, 23; EX1013, 6, 7; EX1084, ¶68; *Section* IV.B. Instead, POSAs would have understood Stelmasiak's "responders" had different weights and Stelmasiak was simply unable to identify any factor differentiating the 'responders' and 'non-responders.'" EX1013, 7; Decision, 43; EX1084, ¶68.

B. The prior art suggests the claimed maintenance period after the claimed cladribine-free period.

Merck wrongly argues against re-treating after Bodor's 10-month cladribine-free period due to cladribine's alleged safety and efficacy concerns. POR, 24-27,

31-32; Decision, 49-50; EX1084, ¶¶11, 74-78. Yet, Bodor discloses a 10-month cladribine-free period specifically for use with its "instant solid dosage form." EX1022, 23:15-20; Pet., 45-52; EX1084, ¶76. And POSAs would have re-treated to maintain the lymphocyte suppression effected during an induction period. EX1084, ¶¶72, 76, 95-96; EX1002, ¶¶90, 109. Further, the art demonstrated cladribine's efficacy and safety. *Section* IV.B. Merck's additional flawed arguments (POR, 24-35) also fail:

1. Other drugs are informative for cladribine.

Merck wrongly contends: (1) Hopewell relied on corticosteroids, cyclophosphamides, and intravenous methylprednisone; and (2) none of the FDA-approved disease-modifying therapies (DMTs, aka DMAs) "was dosed in a 'cyclic' manner." POR, 27-30.

Hopewell did not solely rely on corticosteroids, cyclophosphamide, and methylprednisone for cladribine's dosing. POR, 27 (citing EX1002, ¶¶59, 87), 28. Rather, the art as a whole disclosed cyclical regimens for DMTs (e.g., mitoxantrone, natalizumab), general immunosuppressives (e.g., corticosteroids, cyclophosphamide), ***and*** cladribine. EX1002, ¶¶57-63; Pet., 15-18; EX1084, ¶¶79-80, 95; EX2018; EX2019; EX1008; EX1013; EX1022; EX1023. POSAs would have applied Bodor's and Stelmasiak's suggestions for cladribine retreatment, while considering general knowledge of cyclical regimens. Pet., 15-18; EX1084,

¶79. Undeniably, DMTs were administered cyclically (initial treatment, drug-free period, and retreatment). EX1084, ¶¶79-80; EX2018, 29; EX2019, 10; Pet., 15-18. Merck misrepresents mitoxantrone's "quarterly" dosing and natalizumab's "300 mg once every four weeks" dosing as "continuous" rather than "cyclical." POR, 27-30; EX2051, ¶¶57, 103; EX2051, ¶56; EX2020, 571, 573; EX2019, 10; EX1084, ¶80.

2. Prior art suggests the claimed maintenance period.

Merck mischaracterizes the art and misapplies the law to argue against re-treatment immediately after Bodor's cladribine-free period, incorrectly alleging "most" prior cladribine studies lacked retreatment. POR, 30-33. No law requires that "most" of the art teach or suggest a claim element. Decision, 39. The art is considered as a whole, and even a single reference is sufficient to suggest a claim element. *SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp.*, 225 F.3d 1349, 1356 (Fed. Cir. 2000). Indeed, multiple prior studies re-treated with cladribine. Pet., 19-22; EX1018, 1146; EX1031; EX1013, Abstract, 5; EX1022; EX1002, ¶38-49; EX1084, ¶¶69-70, 75. Retreatment was recommended given cladribine's temporary lymphocyte suppression and MS's chronic nature. EX1084, ¶¶71-73, 95-96.

Merck argues against retreatment, alleging Bodor disclosed no re-treatment criteria and a lack of consensus on when to re-treat. POR, 30-33. But obviousness

does not mandate *Bodor* explicitly provide retreatment criteria. POSAs would have considered general knowledge of retreatment regimens (e.g., Romine, Rice, Stelmasiak). EX1084, ¶75.

As the Board correctly concluded, there is no fixed lymphocyte-reduction "bright-line threshold." Decision, 47; EX1002, ¶¶32, 40, 90; EX1084, ¶¶14, 90. Cladribine's effect was commonly assessed by monitoring lymphocytes, with a sustained reduction, e.g. to ≤ about 1000/μL, reflecting treatment response. EX1002, ¶¶32, 40, 90; EX1084, ¶¶14, 90.

Finally, Merck wrongly argues that POSAs could have instead used other available MS drugs. POR, 33. Even if some clinicians might have switched drugs, the art ***still*** suggested re-treating with cladribine as discussed above. EX1084, ¶73.

3. Merck's argument that Stelmasiak does not suggest the claimed maintenance dose and period is irrelevant.

Hopewell did not argue modifying Bodor's method to incorporate *Stelmasiak's* cladribine-free and lower-dose maintenance periods. Pet., 35-39; Decision, 40-41. Hopewell applied Stelmasiak for suggesting a cyclical regimen and a maintenance dose lower than the induction dose, and then argued routine optimization. *Id.*; EX1084, ¶¶72, 95. Merck also fails to counter Hopewell's routine optimization arguments (*Section* VI.B).

VI. HOPEWELL ESTABLISHED MOTIVATION AND REASONABLE EXPECTATION OF SUCCESS.

Not only should Merck's weight-based and average-weight-patient arguments be rejected (POR, 35-37, 48-49; *Sections* III, IV.A, V.A), so should Merck's other arguments. (EX1080, ¶¶1-83; EX1084, ¶¶1-133):

A. Merck fails to rebut Hopewell's induction dose arguments.

Merck relies on two faulty premises to argue against Bodor's tablets and regimen as a starting point: (1) Bodor's bioavailability was inferior to Stelmasiak's and (2) Bodor's total induction dose was not expected to be effective. POR, 49-53; EX1080, ¶¶1-83.

First, POSAs would have understood that Bodor's bioavailability was at least comparable to Stelmasiak's (Bodor's 35.7-52.1% vs. Stelmasiak's 37-51%), and it was good for an oral dosage form. *Section* IV.C; EX1080, ¶¶34-36, 60-63; EX1084, ¶¶15, 60; EX1002, ¶110; EX1022, EX1013. Even Dr. Bodor (an accomplished scientist, per Meibohm) admits "achiev[ing] at least 30% bioavailability" makes Bodor's tablets a "successful drug." EX1059, 38:18-40:17; EX1062, 72:12-74:8. Similarly, Munafo deemed 35-39% bioavailability a "favorable pharmacokinetic … profile[]." EX1072, Abstract. Also, there was no set bioavailability threshold, and low bioavailability did not compromise drugs' effectiveness. EX1080, ¶¶34-36; EX1078, Table 1. Even Meibohm admits, "there are … approved drugs with a bioavailability of 1 to 2 percent." EX1062, 59:3-14.

Moreover, the law "***does not require*** that a particular combination must be the ***preferred, or the most desirable.***" *Novartis v. West-Ward*, 923 F.3d 1051, 1059 (Fed. Cir. 2019); Decision, 48, fn21. Instead, the prior art as a whole can "***suggest the desirability***." *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004). Merck wrongly focused only on Bodor's bioavailability even though Hopewell identified additional desirable features. Pet., 23, 33-34; EX1002, ¶¶53, 79, 96; EX1084, ¶¶8, 58, 59; EX1080, 16, 17, 37-47; EX1022, 5:4-8, 8:17-24, 11:27-12:3; POR, 49-52, 55-57.

Further, Bodor explicitly teaches its tablets were "well-suited for optimizing the oral bioavailability of cladribine." EX1022, 8:22-30; Pet., 47; EX1080, ¶¶16, 53, 56, 62; EX1002, ¶56, 79; EX1084, ¶58. Bodor noted its tablets had lower interpatient variability, an important factor a POSA would have considered (lower variability provides higher confidence a drug will be consistently effective across patients with decreased unexpected toxicity). Pet., 23; EX1080, ¶¶16, 37-40, 64-65, 83; EX1002, ¶97; EX1084, ¶¶58; EX1069, 605; EX1076, 151. Pinal summarizes Bodor's lower variability compared with prior solutions:

Prior Art	**Interpatient Variability (Coefficient of Variation)**	**Dosage Form**
Bodor	28-30%	Tablet

Prior Art	**Interpatient Variability (Coefficient of Variation)**	**Dosage Form**
Stelmasiak (citing Liliemark 1992)	38%	Oral Solution
Saven	40%	Oral Solution
Albertioni	26-27%	Oral Solution

EX1080, ¶64. [redacted]

POSAs would have preferred tablets over solutions due to their increased stability and shelf-life, increased convenience, patient compliance, safety, and decreased cost. Pet., 22-23; EX1002, ¶58; EX1084, ¶¶58-69, 61; EX1080, ¶¶15-17, 41-27, 51-53, 60, 66-67; EX1064, 581; EX1065, 287; EX1067, 23; EX1076, 154-155; EX1077, 9; Table 3. Tablets were the "Holy Grail," and Bodor's tablets were "especially suited" for oral administration. EX1066; EX1080, ¶¶41, 53, 56, 61-62, 66; EX1002, ¶56; EX1022, Abstract. Even Merck's witnesses admit preferring tablets. EX1059, 59:9-60:14, 61:8-62:14, 63:14-64:14; EX1060, 49:5-13; EX1062, 50:11-52:9.

Second, Merck wrongly argues that given Bodor's lower induction dose (and bioavailability) compared to Stelmasiak, POSAs would not have "start[ed] with Bodor's oral cladribine dose." POR, 51-53; EX1084, ¶¶89-94, 96. As the

Board correctly concluded, there is no fixed lymphocyte-reduction "bright-line threshold." Decision, 47; EX1002, ¶¶32, 40, 90; EX1084, ¶¶14, 90. Instead, cladribine's effect was commonly assessed by monitoring lymphocytes, with a sustained reduction, e.g. to ⩽ about 1000/μL, reflecting treatment response. *Id.* Moreover, Rice reported that cladribine doses similar to Bodor's suppressed lymphocytes to ⩽ about 1000 cells/μL. EX1084, ¶92; EX1080, ¶¶78-83; EX1018, Abstract. Lublin admittedly ignored Rice's data. EX1061, 95:22-96:13; EX1084, ¶¶16, 92. Further, Rice reported lowered brain-lesion numbers and volumes. EX1084, ¶¶16, 51, 93. POSAs would have reasonably expected Bodor's dosing to reduce lymphocytes to ≤ about 1000 cells/μL and reduce the number and/or volume of brain lesions. EX1084, ¶¶16, 93; EX1080, ¶¶78–83.

While ignoring Stelmasiak's "very marked" and successful relapse reduction, Merck also misrepresents Stelmasiak's EDSS. EX1084, ¶¶52, 94, 95; EX1013, 7. Miller and Lublin explain: Stelmasiak's EDSS trend indicates the disease did *not* worsen—a positive outcome. EX1084, ¶¶52, 94-95; EX1061, 57:3-4. No particular efficacy degree or metric(s) is required. *Section* III.

B. Merck fails to undermine routine optimization.

First*,** Merck disputes Hopewell's result-effective variable analysis, arguing lymphocyte count is a metric of cladribine's safety, not efficacy. POR, 37-42, 43. But ***any property reflecting an "effect of the therapy" and known in the art to be

affected by the optimized variable suffices, which is the case here. EX2009, 30:17-31:1; EX2051, ¶137; EX1002, ¶16, 31, 34, 38, 48, 52; EX1084, ¶¶12, 81-88; *DuPont v. Synvina*, 904 F.3d 996, 1009 (Fed. Cir. 2018) ("[A] recognition in the prior art that a property is affected by the variable is sufficient to find the variable result-effective."). Having no meritorious rebuttal, Merck engages in semantics games. POR, 38.

Lublin agrees cladribine reduces lymphocyte counts in a dose-dependent manner. EX1084, ¶¶12, 81, 82; Pet., 19-22; EX1002, ¶105; EX1013, Abstract; EX2051, ¶74; EX2009, 36:5-12; EX1061, 72:19-22. Prior studies routinely used lymphocyte counts to measure cladribine's effect. EX1002, ¶¶40, 48, 92; EX1084, ¶¶25, 26, 50, 92; EX1061, 72:5-13, 77:8-11, 84:13-15; EX1018, FIG. 4. Thus, Hopewell's result-effective variable analysis properly applies lymphocyte counts. Pet., 40-43.

Second, Merck wrongly opposes optimization due to "no guidance" on threshold lymphocyte counts. POR, 41-42. POSAs routinely assessed cladribine's effects using lymphocyte counts. *Section* VI.A. Prior studies (e.g., Rice) reported effects on lymphocyte levels with dosing similar to Bodor's. *Section* VI.A; EX1018, Abstract.

Third, Merck wrongly contends Hopewell argued ***adjusting*** the cladribine dose ***daily***. POR, 43-44. Hopewell and the patent used "daily dose" to mean a dose

that's ***administered daily***. Pet., 23, 59-60; EX1001, 4:18-21, 20:17-22; EX1084, ¶86; POR, 43-44.

Fourth, Merck wrongly argues that cladribine's "treatment benefits" and "clinical outcomes" can only be assessed over years, precluding optimization. POR, 44-45. But, cladribine-dosing adjustments do not require years. EX1084, ¶84. MRIs show treatment responses in ≤ 6 months, and Lublin admits relapse rates typically are measured over a one-year period. EX1084, ¶¶12-13, 83-84; EX1061, 38:10-12; EX1031, 40. As Stelmasiak and Romine demonstrate, changes in lymphocyte levels can be seen within a month or two. EX1084, ¶84; EX1013, FIG. 1; EX1031, FIG. 6.

Finally, while complaining of "numerous possible combinations" for optimization (POR, 45-48), Merck ignores Bodor's explicit disclosure of a 10-month cladribine-free period specifically for its "instant solid dosage form." EX1022, 23:15-20; Pet., 45-52; EX1084, ¶88. POSAs would have followed the maintenance period with a second cladribine-free period to mitigate against any cladribine side-effects (similar to Stelmasiak), optimizing the cladribine-free period's length based on lymphocyte count, reasonably expecting success. Pet., 54; EX1002, ¶¶103-105; EX1084, ¶¶87-88. Multiple prior-art studies showed cladribine effectively treating RRMS. Pet., 19-22, 41; EX1002, ¶¶33-52; EX1084, ¶¶51-52, 106, 122; *Section* IV.B. Merck's reasons for arguing otherwise lack merit.

Section IV.B.

Merck misrepresents EX2031 to argue against motivation and reasonable expectation. POR, 41, 47 (citing EX2031, 753). EX2031's statement relates only to ***progressive*** MS studies, and was not from a POSAs' perspective considering all pertinent art. EX1084, ¶109. There is no evidence the statement considered Bodor or Stelmasiak, and being "convinced" is not the standard for obviousness.

C. Merck fails to rebut Hopewell's re-treatment argument.

The art contradicts Merck's arguments against re-treating patients after Bodor's cladribine-free period (POR, 53-55) and arriving at the claimed maintenance dose (POR, 55-57). *Section* V. POSAs would have considered successful studies that include retreatment, and would have been motivated to re-treat after Bodor's cladribine-free period with a reasonable expectation of success. EX1084, ¶¶69-70, 75; *Sections* VI.A-B.

Further, with proper consideration of Bodor's and Stelmasiak's bioavailability and other data, POSAs would have been motivated to administer the claimed maintenance dose with a reasonable expectation of success. *Sections* V, VI.A-B.

VII. DEPENDENT CLAIMS

Merck's dependent-claims arguments fail for the reasons above. Claim 39 requires a maintenance dose lower than the induction dose. *Section* III; EX1084,

¶98. The Petition's arguments remain applicable to all claims. Pet., 55-60; EX1084, ¶97.

VIII. MERCK'S OBJECTIVE INDICIA FAIL

EX2038 does not evidence **skepticism**. POR, 59-60, 65; EX1084, ¶¶19, 99-100, 114-116. It makes no mention of any FDA "concerns over higher cancer risks." POR, 60; EX2038; EX1084, ¶114. Instead, FDA found CLARITY effective but "requested … an improved understanding of safety risks and the overall benefit-risk profile either through ***additional*** analyses or by ***additional*** studies." EX2038, 1; EX1084, ¶114. This request merely reflects FDA's "attention to [its] normal duties ensuring the safety and efficacy," not skepticism. *Bayer Healthcare v. Watson*, 713 F.3d 1369, 1377 (Fed. Cir. 2013).

Neptune is inapposite. *Neptune Generics v. Eli Lilly*, 921 F.3d 1372, 1378 (Fed. Cir. 2019). There, FDA expressed skepticism regarding proposed ***changes*** to a treatment strategy. *Id.* Here, there is no evidence of FDA concerns vis-a-vis CLARITY's treatment strategy or Merck proposing changes. EX2038, 1; EX1084, ¶114.

Merck also fails to consider all art reporting cladribine's efficacy. EX1084, ¶¶102, 103, 105, 106, 109; EX1013; EX1031. And Merck's EX2004 actually is optimistic about oral cladribine, encouraging additional trials. EX2004, 341; EX1084, ¶¶105-107.

Merck fails to show **unexpectedly superior results**. *In re Merchant*, 575 F.2d 865, 868 (C.C.P.A. 1978) (discussing comparing claim limitations). EX1084, ¶¶118-127. Under *Merchant*, Bodor is the closest prior art: Its induction period overlaps the claimed dose and duration, its cladribine-free period falls within the claimed period, and Bodor suggests re-treatment. Pet., 45-52; EX1084, ¶¶119-123. Neither Stelmasiak nor Romine is closest because Bodor has more elements in common with the claims. EX1084, ¶¶120-123; EX1022; EX1013; EX1031. Yet, Merck did not compare its results with Bodor, only with Romine and Stelmasiak (POR, 61), and Lublin had no concept of "closest prior art." EX1061, 113:4-115:20; EX1084, ¶¶120-123. Merck also misrepresents Stelmasiak's EDSS as poor, when it is the opposite: Stelmasiak's EDSS indicated disease did not worsen. *Section* IV.B.1; EX1084, ¶¶17, 52, 94-95.

Any **long-felt, unmet need** must exist as of the "filing date of the challenged invention." *P & G v. Teva Pharms*., 566 F.3d 989, 998 (Fed. Cir. 2009). But Merck submits irrelevant ***post-filing*** evidence. EX1084, ¶¶128-133; POR, 63; EX2051, ¶211.

Merck fails to establish **nexus** between its evidence and the claims' merits. *Lectrosonics, Inc. v. Zaxcom, Inc*., IPR2018-01129, Paper 33, at 32-33 (P.T.A.B. Jan. 24, 2020) (precedential). There is no presumption of nexus, because Merck's evidence is not nearly coextensive with the claims. *Id.* Merck's ***skepticism***

evidence (EX2004, EX2005, EX2031, and EX2011), except EX2038 (which is irrelevant), relates only to ***progressive*** MS and ***non-oral*** administration. EX1084, ¶¶103-104, 106, 108-112; EX1061, 119:12-20, 123:14-17, 127:1-13. E.g., Miller commented only on ***progressive*** MS in EX2004 and EX2005. EX1084, ¶¶103-106; EX2031, 753. Also, Miller's comments were not offered from a POSA's perspective considering all pertinent art. EX1084, ¶¶103, 105.

Merck's ***unexpected-results*** and ***long-felt-unmet-need evidence*** is based only on MAVENCLAD, which treats ***RRMS*** patients for ***2 years*** with cladribine ***tablets***. EX1084, ¶¶124-125; Decision, 51. But, the claims are broader, encompassing ***any*** type of MS, ***any oral*** cladribine dosage form, and ***any regimen of ≥2 years***. EX1084, ¶125; EX1061, 143:13-16.

Merck alleges its "durable," 2-year regimen is a unique claimed characteristic. POR, 61-62, 63, 64, 65. But none of Merck's evidence is a "direct result" of Merck's regimen rather than prior-art cladribine formulations and regimens. EX1022; EX1013; EX1084, ¶¶113, 126, 130. And Merck admits the durability stems from cladribine's inherently "unique mechanism" as an "immune reconstitution therapy." POR, 62-63; EX2051, ¶¶211-213; EX1084, ¶¶113, 126, 130.

All claims are unpatentable.

Respectfully submitted,

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CERTIFICATE OF WORD COUNT (37 C.F.R. § 42.24(d))

1. This Petitioner's Reply complies with the type-volume limitation of 5,600 words, comprising 5,568 words, excluding the parts exempted by 37 C.F.R. § 42.24(c).

2. This Petitioner's Reply complies with the general format requirements of 37 C.F.R. § 42.6(a) and has been prepared using Microsoft® Word 2016 in 14-point Times New Roman font.

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CERTIFICATE OF SERVICE (37 C.F.R. § 42.6(e))

I certify that the above-captioned **PETITIONER'S REPLY TO PATENT OWNER RESPONSE** and associated Exhibits 1055-1081 and 1083-1084 were served in their entireties on April 5, 2024, upon the following parties via email:

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