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Paper 13
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COALITION FOR AFFORDABLE DRUGS (ADROCA) LLC,
Petitioner,

v.

ACORDA THERAPEUTICS, INC.,
Patent Owner.

Case IPR2015-01853
Patent 8,007,826 B2

Before MICHAEL P. TIERNEY, LORA M. GREEN, and JACQUELINE WRIGHT BONILLA, *Administrative Patent Judges.*

BONILLA, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Coalition for Affordable Drugs (ADROCA) LLC ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–3, 5–8, and 10–41 of U.S. Patent No. 8,007,826 B2 (Ex. 1001, "the '826 patent"). Paper 2 ("Petition" or "Pet."). Acorda Therapeutics, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp."). Under 35 U.S.C. § 314, 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."

Upon consideration of information presented in the Petition and the Preliminary Response, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–3, 5–8, and 10–41 of the '826 patent. We institute *inter partes* review of those claims.

A. Related Proceedings

The parties identify a number of judicial matters involving the '826 patent, including, among others, *Acorda Therapeutics, Inc. v. Mylan Pharms. Inc.*, No. 1:14-cv-00935 (D. Del); *Acorda Therapeutics, Inc. v. Mylan*, No. 1:14-cv-00139 (N.D.W.Va.); *Acorda Therapeutics, Inc. v. Accord and Intas*, No. 1:14-cv-00932 (D. Del.); and *Acorda Therapeutics Inc. v. Mylan Pharm. Inc.*, Case 15-124 (Fed. Cir.). Pet. 2–3; Paper 5, 2–5.

The parties also identify Case No. IPR2015-00817, previously denying *inter partes* review of the same challenged claims in the '826 patent, as well as Case No. IPR2015-00720, previously denying *inter partes* review of challenged claims in a related child patent, U.S. Patent No. 8,663,685, ("the '685 patent"). Petitioner also filed three other Petitions for

inter partes review, one involving the '685 patent (Case No. IPR2015-01857), and two involving patents directed to similar subject matter, i.e., U.S. Patent No. 8,440,703 (Case No. IPR2015-01850) and its parent U.S. Patent No. 8,354,437 (Case No. IPR2015-01858). *Id.*

B. Proposed Ground of Unpatentability

Petitioner advances one ground of unpatentability under 35 U.S.C. § 103(a) in relation to the challenged claims in the '826 patent (Pet. 21, 33–57):

References	Statutory Basis	Challenged Claims
S-1 (Ex. 1003)[1] and Hayes (Ex. 1005)[2]	§ 103(a)	1–3, 5–8, and 10–41

In addition, Petitioner supports its challenges with Declarations by Scott Bennett ("Bennett Declaration") (Ex. 1016), Samuel J. Pleasure, M.D., Ph.D. ("Pleasure Decl.") (Ex. 1023), and James Polli, Ph.D. ("Polli Decl.") (Ex. 1049). Pet. ix–xi.

C. The '826 Patent

The '826 patent relates to methods of using a sustained release oral dosage form of an aminopyridine composition to treat a neurological disorder, such as multiple sclerosis ("MS"), by maximizing the therapeutic effect, while minimizing adverse side effects. Ex. 1001, 1:16–25.

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[1] *Form S-1 Registration Statement Under the Securities Act of 1933*, Acorda Therapeutics, Inc. (filed Sept. 26, 2003) ("S-1") (Ex. 1003).

[2] Hayes et al., *Pharmacokinetic Studies of Single and Multiple Oral Doses of Fampridine-SR (Sustained-Release 4- Aminopyridine) in Patients With Chronic Spinal Cord Injury*, 26(4) CLINICAL NEUROPHARMACOLOGY 185–92 (2003) ("Hayes") (Ex. 1005).

Examples 4 and 5 in the ’685 patent present pharmacokinetic parameters of fampridine (4-aminopyridine) compositions administered to patients with MS. *Id*. at 19:56–22:32. In Example 8, the ’826 patent describes a clinical trial “to evaluate safety, tolerability and activity of oral fampridine-SR [sustained release] in subjects with Multiple Sclerosis.” *Id*. at 25:52–56. As stated in Example 8, “the Timed 25 Foot Walk is widely-used to assess MS patients’ functional status.” *Id*. at 26:37–40. The trial “showed a strong positive trend across all three dose groups compared to placebo in its primary endpoint, improvement in walking speed, as measured by a timed 25-foot walk as shown in FIG. 3.” *Id*. at 26:29–32. In addition, the trial “showed a statistically significant improvement across dose groups in its secondary endpoint, the Lower Extremity Manual Muscle Test (LEMMT), as shown in FIG. 4.” *Id*. at 26:32–35. The ’826 patent further states that this study “confirms the safety profile of 4-aminopyridine and preferable dosing of 10 to 15 milligrams twice daily.” *Id*. at 26:46–48.

D. Illustrative Claims

Claims 1, 6, 11, 17, 31, 36, and 37 are independent claims in the ’826 patent. Claims 1 and 31, reproduced below, are representative.

> 1. A method for maintaining a therapeutically effective concentration of 4-aminopyridine in order to improve walking in a human with multiple sclerosis in need thereof, said method comprising:
>
> orally administering to the human a sustained release composition of 10 milligrams of 4-aminopyridine twice daily for a day; and thereafter,
>
> maintaining administration of 4-aminopyridine by orally administering to said human a sustained release composition of 10 milligrams of 4-aminopyridine twice daily for a time period of at least two weeks, whereby an in vivo 4-aminopyridine C_{maxSS}:C_{minSS}

> ratio of 1.0 to 3.5 and a C_{avSS} of 15 ng/ml to 35 ng/ml are obtained in the human.
>
> 31. A method of increasing walking speed in a human multiple sclerosis patient in need thereof comprising orally administering to said patient a sustained release composition of 10 milligrams of 4-aminopyridine twice daily for a time period of greater than two weeks, wherein said sustained release composition provides a mean T_{max} in a range of about 1 to about 6 hours after administration of the sustained release composition to the patient.

Ex. 1001, 27:17–30, 29:16–23.

II. ANALYSIS

A. Claim Construction

Neither party provides construction of terms in the challenged claims, except that Petitioner contends that the phrase "to improve walking" means "to quantifiably make better a patient's ability to walk." Pet. 21; Prelim. Resp. 24 n.5. We determine that express claim construction of terms is not necessary to our analysis on whether to institute. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (stating that "claim terms need only be construed 'to the extent necessary to resolve the controversy'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

B. The S-1 (Ex. 1003) as "Printed Publication" Prior Art under 35 U.S.C. §102

35 U.S.C. § 311(b) states that a "petitioner in an *inter partes* review may request to cancel . . . claims of a patent only on a ground that could be raised under section 102 or 103 and only on the basis of prior art consisting of patents or printed publications." Before considering Petitioner's obviousness ground, we must address whether a cited reference, the S-1, is prior art under 35 U.S.C. § 102—a legal question based on underlying

factual determinations. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568 (Fed. Cir. 1987); *Kyocera Wireless Corp. v. Int'l Trade Comm'n*, 545 F.3d 1340, 1350 (Fed. Cir. 2008).

The Federal Circuit has held that "public accessibility" is the touchstone in determining whether a reference is a "printed publication" under § 102. *In re Hall*, 781 F.2d 897, 898–99 (Fed. Cir. 1986). "A reference is publicly accessible 'upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it . . . .'" *Kyocera*, 545 F.3d at 1350 (quoting *SRI Int'l, Inc. v. Internet Sec. Sys. Inc.*, 511 F.3d 1186, 1194 (Fed. Cir. 2008)); *In re Lister*, 583 F.3d 1307, 1315 (Fed. Cir. 2009).

A party seeking to introduce a reference "should produce sufficient proof of its dissemination or that it has otherwise been available and accessible to persons concerned with the art to which the document relates and thus most likely to avail themselves of its contents." *In re Wyer*, 655 F.2d 221, 227 (CCPA 1981) (quoting *Philips Elec. & Pharm. Indus. Corp. v. Thermal & Elecs. Indus., Inc.*, 450 F.2d 1164, 1171 (3d Cir. 1971)). As explained by the Federal Circuit, a "determination of whether a reference is a 'printed publication' under 35 U.S.C. § 102(b) involves a case-by-case inquiry into the facts and circumstances surrounding the reference's disclosure to members of the public." *In re Klopfenstein*, 380 F.3d 1345, 1350 (Fed. Cir. 2004).

Petitioner asserts that the S-1 constitutes prior art under 35 U.S.C. § 102(b) because it was published at least as early as September 30, 2003, i.e., more than one year before the earliest effective filing date of the '826

patent. Pet. 23–28. Petitioner argues that the effective filing date of the '826 patent is December 13, 2004, the filing date of the non-provisional application that matured into the patent, not the filing date of related provisional applications filed on December 11, 2003, or April 9, 2004. *Id*. at 11–19. Even assuming the effective filing date for the '826 patent is December 11, 2003, or April 9, 2004, however, Petitioner asserts that the S-1 constitutes prior art in relation to the challenged claims under 35 U.S.C. § 102(a). *Id*. at 23–24; *see also* Prelim. Resp. 10 n.2 (stating that Patent Owner does not address arguments regarding an effective filing date in its Preliminary Response, but reserves the right to do so during trial).

Regarding the S-1, Petitioner asserts that as early as 2000, a person of ordinary skill in the art ("POSA") would have known that Patent Owner was investigating fampridine (4-aminopyridine or "4-AP") "for the potential treatment of spinal cord injuries and multiple sclerosis." *Id*. at 24 (quoting Ex. 1017, 1).[3] Petitioner also contends that news publications dated before the September 2003 filing date of the S-1 indicated to the public that Patent Owner had engaged in clinical trials for the treatment of MS using Fampridine-SR (sustained release). *Id*. at 24–25 (citing Ex. 1018, 1; Ex. 1019, 1). For example, Petitioner points to a "BioSpace" publication dated May 9, 2003, stating that Patent Owner's "lead product, Fampridine-SR, is in Phase 3 clinical trials for chronic SCI and Phase 2 for MS," and stating that Patent Owner is "conducting a 152 patient, late Phase 2 clinical study in

[3] Abstract, 1(3) CURR. OPIN. INVESTIG. DRUGS 375–79 (Nov. 2000) (obtained from PubMed at http://www.ncbi.nlm.nih.gov/pubmed/11249722) (Ex. 1017).

MS to evaluate Fampridine SR's efficacy in walking speed and muscle strength." *Id*. at 24; Ex. 1019, 1.

Petitioner contends that based on such publications, an ordinary artisan would have been motivated to look for information and documents, including U.S. Securities and Exchange Commission ("SEC") filings, such as the S-1 pertaining to an initial public offer of stock, discussing Patent Owner's activities, such as clinical trials studying the effect of Fampridine SR in MS patients. Pet. 24–25 (citing Ex. 1023 ¶¶ 59–60). Petitioner also contends that the S-1 was publicly available online in the SEC's Electronic Data Gathering, Analysis, and Retrieval ("EDGAR") system by at least September 30, 2003. *Id*. at 25–26.

In support, Petitioner relies on a Declaration by Mr. Bennett, an academic librarian, who states that, by law, U.S. companies making an initial public offering of stock must file certain forms, including an S-1 form, with the SEC, and since 1996, those filings have been available to the public in the SEC's EDGAR system. *Id*. at 25–26; Ex. 1016 ¶¶ 2, 11, 12. Mr. Bennett refers to Attachment 3 to his Declaration as presenting "EDGAR Filing Details" for the S-1, and showing that "the SEC filed [Patent Owner's S-1] document and its exhibits on EDGAR on 29 September 2003." Ex. 1016 ¶ 15 (referring to Ex. 1032 ("Attachment 3")). Petitioner also refers to an "SEC News Digest" (or "SEC Digest") dated September 30, 2003, which includes a listing of "Security Act Registrations." Pet. 26; Ex. 1004, 9. According to Petitioner, that "SEC Registration Statement [] provided instructions to the public for obtaining a printed copy of the *S-1* publication via mail, further establishes its public availability." Pet. 26.

In response, Patent Owner contends that the S-1 was not a "printed publication," as required under 35 U.S.C. § 311(b). Prelim. Resp. 9–16. Patent Owner argues that the S-1 document was not "sufficiently accessible to the public interested in the art" in 2003. *Id*. at 9–10, 11 (quoting *Klopfenstein*, 380 F.3d at 1348). Patent Owner contends that "Petitioner has provided no evidence that the S-1 was indexed or cataloged in the SEC's EDGAR database in a way that would have made it sufficiently accessible to those of ordinary skill in the art." *Id*. at 12. Patent Owner argues that "EDGAR only adopted full-text keyword searching in 2006, after the priority date of the claimed invention," and therefore not was "like the 'automated catalog' in *Lister* or the library in *Cronyn*, which the Federal Circuit held were not sufficiently accessible." *Id*. at 12–13 (citing Ex. 2003; *In re Lister*, 583 F.3d 1307, 1315 (Fed. Cir. 2009) (indexing a computer database by author and first word in the title); *In re Cronyn*, 890 F.2d 1158, 1161 (Fed. Cir. 1989) (indexing theses by student's name)).

Patent Owner also refers to a Decision by a different Board panel in *Liberty Mutual Insurance Co. v. Progressive Casualty. Insurance Co.*, CBM2013-00009, Paper 68 (PTAB Feb. 11, 2014) ("*Liberty Mutual*"), which addresses the public accessibility of an SEC 10-K annual report. Prelim. Resp. 13–14. Citing that Decision, Patent Owner suggests that an SEC document, such as the S-1 here, cannot be sufficiently publicly accessible unless it is indexed or catalogued at the SEC "based on the technical content contained therein." *Id*. (quoting *Liberty Mutual*, slip op. at 18). According to Patent Owner, because one could only search EDGAR based on a company name in 2003, and could not do "full-text keyword searching" or searching "based on the technical nature contained therein" at

that time, the S-1 was not sufficiently publicly accessible to qualify as a printed publication in 2003. *Id*. at 12–14.

Regarding the SEC Digest, Patent Owner contends that it merely lists the name and address of Patent Owner, and "says nothing about the content of the S-1, or whether it contains information regarding the treatment of MS," and, therefore, does not provide "the opportunity to access the S-1 for 'the technical content contained therein.'" *Id*. at 16 (quoting *Liberty Mutual*, slip op. at 18).

As noted above, whether a reference is publicly accessible is determined on a case-by-case basis based on the facts and circumstances surrounding disclosure of the reference to the public. *Lister*, 583 F.3d at 1311. Based on the information before us, we are persuaded that Petitioner has provided a sufficient showing that the S-1 was publicly accessible to the public interested in the art as of September 30, 2003.

The SEC Digest dated September 30, 2003, which includes a list of registration statements, including Patent Owner's S-1, indicates to the public how to obtain such statements. As noted by Patent Owner, the SEC Digest refers to Patent Owner's company name and address in the portion that lists Patent Owner's S-1 document. Prelim. Resp. 16; Ex. 1004, 9. Just above that disclosure, the SEC Digest also states:

> The following registration statements have been filed with the SEC under the Securities Act of 1933. . . .
>
> Registration statements may be obtained in person or by writing to the Commission's Public Reference Branch at 450 Fifth Street, N.W., Washington, D.C. 20549 or at the following e-mail box address: <publicinfo@sec.gov>. In most cases, this information is also available on the Commission's website: <www.sec.gov>.

Ex. 1004, 9. We are persuaded that Petitioner establishes sufficiently that the SEC Digest explains how to obtain a copy of the S-1, as of the SEC Digest's publication date of September 30, 2003.

In addition, the record before us supports Petitioner's contention that public documents available before September 2003 indicated to an ordinary artisan that Patent Owner's "lead product" was a sustained release form of 4-aminopyridine, i.e., Fampridine-SR, and that Patent Owner was testing that product in clinical trials to evaluate its effect on walking speed and muscle strength in MS patients. Ex. 1017, 1; Ex. 1019, 1. We are persuaded that Petitioner establishes sufficiently that such documents would have prompted a person of ordinary skill interested in the art to look for other publicly available information relating to Patent Owner and its activity, including SEC documents, such as the S-1, via EDGAR. Petitioner also establishes sufficiently that an ordinary artisan looking for such documents could have located the S-1 upon exercising reasonable diligence, for example, in view of EDGAR and the SEC Digest, as discussed above.

Although the *Liberty Mutual* decision is not binding on this panel, we note that the information before us is distinguishable from that at issue in *Liberty Mutual*. For example, *Liberty Mutual* states that the petitioner in that case "explains little, if anything, about how '10-K' forms are indexed or catalogued at the Security and Exchange Commission, or how else the public may search the 10-K forms based on the technical content contained therein." *Liberty Mutual*, slip op. at 18. In other words, unlike here, the petitioner in *Liberty Mutual* provided little to no information as to how one could locate the 10-K form at the SEC by any means. We do not read the panel in *Liberty Mutual* to say that the ability to search an SEC form "based

on the technical content contained therein" is a requirement for such a form to qualify as a printed publication in every factual circumstance, regardless of whether other means exist to allow one to locate the document upon exercising reasonable diligence. Here, Petitioner reasonably points to EDGAR and the SEC Digest as providing available means to locate and obtain a copy of the S-1.

The S-1 is Patent Owner's own document. Patent Owner will have a full opportunity during trial to submit additional evidence regarding the publication of the S-1, its public accessibility, and information it contains regarding the Fampridine-SR MS clinical trials.

C. 35 U.S.C. § 325(d)

Patent Owner asks us to exercise our discretion to deny institution of a trial in this case under 35 U.S.C. §§ 314(a) and 325(d). Prelim. Resp. 18–23. Patent Owner argues that prior art references asserted in the current Petition also were asserted or cited by the same Petitioner challenging the same claims in a Petition that we denied in an earlier case. *Id*. at 18–19 (referring to *Coalition for Affordable Drugs (ADROCA) LLC v. Acorda Therapeutics, Inc.*, Case No. IPR2015-00817, Paper 1 (Petition) and Paper 12 (Decision denying institution) (PTAB Aug. 24, 2015) ("Prior Decision")).

In that Prior Decision, however, we denied institution on the basis that grounds in the earlier Petition relied on two posters, and Petitioner failed to make a threshold showing that either poster was sufficiently publicly accessible to qualify as a "printed publication" under § 102(b). Prior Decision, slip op. at 2–6. Thus, we did not address whether the S-1 qualified as a "printed publication" under § 102(b), nor whether information before us

established a reasonable likelihood that Petitioner would prevail in an obviousness challenge based on the S-1. In view of the circumstances in this case, which differ from those in cases cited by Patent Owner (Prelim. Resp. 20–23), we decline to deny institution under § 314(a) and § 325(d).

D. Asserted Obviousness Over the S-1 and Hayes

Petitioner asserts that claims 1–3, 5–8, and 10–41 of the '826 patent would have been obvious over the S-1 in view of Hayes. Pet. 33–57.

1. The S-1 (Ex. 1003)

The S-1 discloses that Patent Owner's "lead product candidate, Fampridine-SR, is a sustained release, oral tablet formulation of fampridine, suitable for twice daily dosing." Ex. 1003, 34.[4] The S-1 refers to "two Phase 3 clinical trials of Fampridine-SR for chronic SCI, and one Phase 2 clinical trial for MS," and how Patent Owner had "performed a series of clinical trials of Fampridine-SR in chronic SCI and MS to establish the pharmacokinetics, safety, and optimal dosing of the drug, as well as to assess its efficacy." *Id*.

In relation to the use of "Fampridine-SR in Multiple Sclerosis," the S-1 discusses two clinical trials, the "current late Phase 2 clinical trial, MS-F202," and an earlier "double-blind Phase 2 clinical trial of Fampridine-SR in Multiple Sclerosis, MS-F201," completed in 2001. *Id*. at 37.

In relation to the on-going MS-F202 trial involving 200 patients, the S-1 states that it was "designed to compare three doses of 10, 15 and 20 mg, twice per day, and to assess their relative safety and efficacy over a treatment period of 12 weeks," where the "primary endpoint of the study is

[4] We cite exhibit page numbers as indicated by Petitioner on the bottom right of Exhibit 1003, rather than page numbers designated in the S-1 itself.

an improvement in average walking speed using the Timed 25 Foot Walk." *Id*. The S-1 further states "[i]t is also possible that the clinical trial may not provide statistical significance on the primary endpoint but give us a clear indication of dose and group size to inform the design of two subsequent Phase 3 clinical trials that should provide sufficient pivotal data for submission of the MS NDA." *Id*.

The S-1 states that the prior MS-F201 trial involved 36 patients, 25 of whom "received Fampridine-SR in doses increasing from 10 mg to 40 mg twice per day over eight weeks of treatment." *Id*. That trial "was designed to determine the optimal dose level of Fampridine-SR and to evaluate possible ways in which to measure the effect of the drug on symptoms of the disease, including motor strength, timed walking, and self-reported fatigue." *Id*.

The S-1 discloses that the MS-F201 "trial demonstrated that doses up to 25 mg twice a day were well tolerated, and were associated with statistically significant improvements in walking speed and leg muscle strength," and that "[m]ost of the improvement in strength and walking speed was apparent within the first three weeks of the Fampridine-SR treatment, at doses from 10 to 25 mg twice a day." *Id*.

In relation to the MS-F201 trial, the S-1 further states:

> When we examined the measurements from individual subjects, and looked at the improvement in walking speed between the baseline period and the average over the first four treatment weeks, we found clear differences in the pattern of response between Fampridine-SR and placebo-treated subjects, as shown in Figure 2. The placebo-treated subjects showed some tendency to improve or worsen slightly in walking speed, mostly within 20% of their baseline average. However, the Fampridine-SR treated group showed a marked tendency for

> improvement in speed, with 9 of 25 subjects improving more than 20% from baseline, and 2 with greater than 50% improvement.

Id. (referring to Figure 2, *id*. at 37–38).

2. Hayes (Ex. 1005)

Hayes is entitled "Pharmacokinetic Studies of Single and Multiple Oral Doses of Fampridine-SR (Sustained-Release 4-Aminopyridine) in Patients With Chronic Spinal Cord Injury." Ex. 1005, 1.[5] Hayes states that "[t]wo studies were conducted to determine the pharmacokinetics and safety profile of an oral, sustained-release (SR) formulation of fampridine (fampridine-SR, 10–25 mg) administered as a single dose (n = 14) and twice daily for 1 week (n = 16) in patients with chronic, incomplete SCI," i.e., spinal cord injury. *Id*. at 1, Abstract.

Hayes discloses that "[c]linical trials have confirmed that administration of fampridine results in symptomatic improvements in patients with SCI and multiple sclerosis." *Id*. at 1 (citations omitted). Hayes discusses its "first study [that] evaluated single oral doses of fampridine-SR (10 mg, 15 mg, 20 mg, and 25 mg) in 14 patients with SCI," and its "second study [that] examined multiple oral doses (10 mg, 15 mg, 20 mg, and 25 mg, twice daily, each given for 1 week) of fampridine-SR in 16 patients with SCI." *Id*. at 2.

In relation to the second study, Hayes discloses that 16 patients "received doses of orally administered fampridine-SR tablets at each dose level (10, 15, 20, and 25 mg) twice daily for 6 consecutive days and then once daily on the seventh day," and "[d]osing at each level was performed in

[5] We cite exhibit page numbers as indicated by Petitioner on the bottom right of Exhibit 1005, rather than page numbers designated in Hayes itself.

an ascending manner over 4 weeks with no intervening washout period." *Id*. Thus, at one point, patients received 10 mg of Fampridine-SR tablets twice daily for six days as part of this study.

In relation to a number of measured pharmacokinetic parameters in the second study, as presented in Figure 1B and Table 3, Hayes states that "[s]teady state was achieved by day 5 (4 days of fampridine-SR dosing) after twice-daily administration of fampridine-SR." *Id*. at 4. Figure 1B presents the mean fampridine plasma concentration versus time over 24 hours for each dosage, including 10 mg, given twice daily. *Id*. at 5. Table 3 presents the "Mean (±standard deviation) pharmacokinetic parameters of fampridine-SR after multiple-dose administration" for each dosage, including 10 mg given twice daily. *Id*. at 7. Such parameters for the 10 mg dosage twice daily dosage include: C_{maxss}, ng/mL of 32.2 ± 8.9, C_{minss}, ng/mL of 14.0 ± 4.4, C_{avss}, ng/mL of 20.8 ± 5.7, and t_{max}, h of 2.7 ± 1.0. *Id*.

3. Analysis

For purposes of institution, based on the record before us, we are persuaded that Petitioner is reasonably likely to succeed in showing that the S-1 expressly discloses or suggests all limitations of the challenged claims except the pharmacokinetic limitations recited in the independent claims. Pet. 33–57. The pharmacokinetic limitations include "whereby an in vivo 4-aminopyridine C_{maxSS}:C_{minSS} ratio of 1.0 to 3.5 and a C_{avSS} of 15 ng/ml to 35 ng/ml are obtained in the human," as recited in claims 1, 6, 11, 17, and 36, and "wherein said sustained release composition provides a mean T_{max} in a range of about 1 to about 6 hours [or about 2 to about 5.2 hours] after administration of the sustained release composition to the patient," as recited in claims 31 and 37, respectively. Ex. 1001, cols. 27–30.

In its Preliminary Response, Patent Owner contends that "the Petition presents the S-1 in a misleading way." Prelim. Resp. 25. For example, according to Patent Owner, the S-1 actually presents "[t]he lone completed clinical MS trial described in the S-1, MS-F201" "as an escalating dose study [that] was not designed to, and did not, evaluate efficacy at any particular dose." *Id*. at 26, 5. Patent Owner contends that statements in the S-1 regarding "statistically significant improvements in walking speed and leg muscle strength," as found in the MS-F201 trial, "do not mean that one could infer the safety or efficacy of the twice daily 10 mg dosages in particular," because those "statements refer to the *aggregate* of all dosages up to and including 25 mg twice a day." *Id*. at 26–27.

Patent Owner also refers to statements in the S-1 regarding the on-going MS-F202 trial, and argues that it "relates to the test methodology chosen for the MS-F202 study, and does not state or even indicate that the data that that trial might generate (in the future) would necessarily support the proposed label indication." *Id*. at 28, 6–7. Patent Owner refers to where the S-1 states, for example, that another clinical trial will be done "as soon as possible to provide the *necessary confirmation*," and it "is also possible that *the clinical trial may not provide statistical significance* on the primary endpoint." *Id*. at 28–29 (quoting Ex. 1003, 37). According to Patent Owner, "[a]t most, the S-1 articulates a hope that a not-yet-completed clinical study would be successful and provide a basis for further development," which is insufficient to establish efficacy of any particular dosage or establish any expectation of success in showing efficacy of the claimed 10 mg twice a day dosage. *Id*. at 29–31.

As discussed above, however, the S-1 states, in relation to results in the MS-F201 trial, that "doses up to 25 mg twice a day were well tolerated, and were associated with statistically significant improvements in walking speed and leg muscle strength," with "[m]ost of the improvement in strength and walking speed was apparent within the first three weeks of the Fampridine-SR treatment, at doses from 10 to 25 mg twice a day." Ex. 1003, 37. We are persuaded, based on the record before us, that Petitioner is reasonably likely to succeed in showing that it would have been obvious to an ordinary artisan reading the S-1 to administer 10 mg of 4-aminopyridine (Fampridine-SR) twice daily for longer than one week, including for "a time period of greater than two weeks," in a method to improve walking or increase walking speed in MS patients, as recited in the challenged claims. Pet. 33–46 (citing paragraphs in the Declaration by Dr. Pleasure (Ex. 1023) in support, for example).

Based on the record before us, we are persuaded that the S-1 suggests such a method, as well as a reasonable expectation of success in performing that method, even if the S-1 does not unequivocally establish the efficacy of the 10 mg twice-per-day dosage, as determined in Phase 2 and 3 clinical trials conducted for market approval by the U.S. Food and Drug Administration. Pet. 35–42 (citing Ex. 1003, 30, 33–35, 37, 45; Ex. 1023 ¶¶ 29, 60–63, 75–89, 93, 97, 118). At this point, it is enough that the S-1 suggests that such a method would work, not least of which because the S-1 refers to an on-going expanded clinical trial, and Patent Owner's plans to engage in further clinical trials, in relation to a 10 mg twice-per-day dosage given over a period of 12-week, in particular, for the treatment of MS. Ex. 1003, 37.

We also are persuaded, based on the record before us, that Hayes indicates that administration of 10 mg of 4-aminopyridine (Fampridine-SR) given twice daily achieves "steady state" after 4 days of dosing, and, at that point, meets the pharmacokinetic limitations recited in the independent claims, as determined from data presented in Table 3 of Hayes, as Petitioner contends. Ex. 1005, 3, 7; Pet. 42–45 (also citing paragraphs in Declarations by Dr. Pleasure (Ex. 1023) and Dr. Polli (Ex. 1049) in support). Petitioner also establishes sufficiently that one would have considered the teachings in Hayes in relation to pharmacokinetic parameters observed when administering 10 mg of 4-aminopyridine twice daily to treat symptoms of MS, as taught in the S-1, even if Hayes discloses results from studies in patients with chronic spinal cord injury (also discussed in the S-1). Pet. 45, 52.

Patent Owner also contends that post-filing results of the MS-F202 study belies any notion that there was an expectation of success in the efficacy of the recited 10 milligram twice a day dosage. Prelim. Resp. 30–31, 6–7. In particular, Patent Owner states that it needed to employ an "innovative responder analysis" to "reveal the efficacy of the claimed 10 mg BID dose." *Id*. An invention is not patentable, however, if it "would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103. Accordingly, we consider knowledge that an ordinary artisan possessed at the time of the effective filing date of the '826 patent. On the record before us at this time, Patent Owner has not persuaded us that an ordinary artisan would have known of its post-filing results when Patent Owner filed its application for the '826 patent.

Based on the record and information before us at this time, we are persuaded to go forward with a trial in relation to claims 1–3, 5–8, and 10–41 of the ’826 patent. Having considered the information and arguments presented in the Petition and Preliminary Response, we are persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge of claims 1–3, 5–8, and 10–41 on the basis of obviousness over the S-1 in view of Hayes.

III. CONCLUSION

For the foregoing reasons, based on the present record, we determine that Petitioner has demonstrated that there is a reasonable likelihood that it would prevail in showing that claims 1–3, 5–8, and 10–41 of the ’826 patent are unpatentable. At this stage of the proceeding, the Board has not made a final determination with respect to the patentability of those challenged claims or any underlying factual or legal issues.

IV. ORDER

Accordingly, it is

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review is instituted as to the ground of unpatentability that claims 1–3, 5–8, and 10–41 of the ’826 patent would have been obvious over the S-1 in view of Hayes; and

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

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