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Paper 9
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIOMARIN PHARMACEUTICAL INC.
Petitioner

v.

GENZYME THERAPEUTIC PRODUCTS LIMITED PARTNERSHIP
Patent Owner

Case IPR2013-00537
Patent 7,655,226 B2

Before LORA M. GREEN, JACQUELINE WRIGHT BONILLA, and SHERIDAN K. SNEDDEN, *Administrative Patent Judges.*

SNEDDEN, *Administrative Patent Judge*.

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

I. INTRODUCTION

BioMarin Pharmaceutical Inc. ("Petitioner") filed a petition to institute an *inter partes* review of claims 1 and 3-6 (Paper 1; "Pet.") of Patent No. 7,655,226 B2 (Ex. 1065; "the '226 patent"). Genzyme Therapeutic Products Limited Partnership ("Patent Owner") filed a preliminary response (Paper 8, "Prelim. Resp.").

The Board has jurisdiction under 35 U.S.C. § 314. The standard for instituting an *inter partes* review is set forth in 35 U.S.C. § 314(a), which states:

> THRESHOLD.—The Director may not authorize an inter partes review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.

Upon consideration of the above-mentioned petition, the Board concludes that Petitioner has established that there is a reasonable likelihood that it will prevail with respect to at least one challenged claim. The Board therefore grants the petition to institute an *inter partes* review.

A. Related Proceedings

Petitioner indicates that there are no other judicial or administrative matters that would affect, or be affected by, a decision in this proceeding. Pet. 1. On the same day Petitioner filed its petition in this proceeding, however, it also filed two other petitions seeking *inter partes* review of U.S. Pat. No. 7,351,410 ("the '410 patent") (IPR2013-00534) and U.S. Pat. No. 7,056,712 ("the '712 patent") (IPR2013-00535). The '226 patent is a continuation of the '410 patent. Although the '712 patent is not related to the '410 patent or the '226 patent, all three patents relate to similar subject matter, i.e., methods of treating Pompe's disease.

B. The '226 Patent (Ex. 1065)

The technology of the patent is enzyme-replacement therapy for patients with Pompe's disease, which is caused by deficiency of the lysosomal enzyme acid alpha glucosidase. Ex. 1065, col. 1, l. 62 to col. 2, l. 10. The patent discloses a method for treating Pompe's disease comprising administering to the patient a therapeutically effective amount of human acid alpha glucosidase. *Id.* The amount is preferably 1-10 mg of enzyme per kilogram of body weight, which may be administered weekly or two weeks apart. *Id.*; *see also, id.* at col. 24, ll. 22-23. The claimed treatment results in the arrest or reduction of clinical and biochemical characteristics of Pompe's disease, which include, generally, an accumulation of glycogen in various tissues such as heart and skeletal muscle, and more specifically, hypertrophic cardiomyopathy. *Id.* at col. 14, l. to col. 15, l. 43.

C. Independent Claims

Claims 1 and 6 are the independent claims of the '226 patent, and are reproduced below:

> 1. A method of treating a human patient with Pompe's disease, comprising administering intravenously to the patient a therapeutically effective amount of human acid alpha glucosidase, whereby the concentration of accumulated glycogen in the patient is reduced and/or further accumulation of glycogen is arrested.
>
> 6. A method of treating a human patient with Pompe's disease, comprising intravenously administering biweekly to the patient a therapeutically effective amount of human acid alpha glucosidase, whereby hypertrophic cardiomyopathy in the patient is reduced and/or arrested.

Claims 3-5 depend on claim 1.

D. The Prior Art

Petitioner relies on the following prior art:

Duke University, "Duke Obtains FDA Designation for Pompe Disease Therapy," press release dated September 2, 1997, 2 pages (Ex. 1002).

Barton et al., "Replacement Therapy for Inherited Enzyme Deficiency – Macrophage-Targeted Glucocerebrosidase for Gaucher's Disease," 324 N. ENG. J. MED. 1464-1470 (1991) (Ex. 1004).

Reuser et al., WO 97/05771, published Feb. 20, 1997 (Ex. 1005).

Van Hove et al., "Purification of recombinant human precursor acid α-glucosidase," 43(3) BIOCHEM. MOL. BIOL. INT. 613-23 (1997) (Ex. 1012).

Van der Ploeg et al., "Receptor-Mediated Uptake of Acid α-Glucosidase Corrects Lysosomal Glycogen Storage in Cultured Skeletal Muscle," 24(1) PEDIATRIC RESEARCH 90-94 (1988) (Ex. 1032).

E. The Asserted Grounds

Petitioner challenges claims 1-6 of the '226 patent on the following grounds. Pet. 33-51.

Reference[s]	**Basis**	**Claim challenged**
Duke Press Release 1997	§ 102(b)	1 and 3
Duke Press Release 1997, Reuser, and Van Hove	§ 103(a)	1 and 3
Duke Press Release 1997, Reuser, Barton, and Van der Ploeg	§ 103(a)	4-6
Duke Press Release 1997 and Reuser	§ 103(a)	1 and 3

II. ANALYSIS

A. Claim Interpretation

Consistent with the statute and legislative history of the America Invents Act (AIA), the Board interprets claims using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *see also Office Patent Trial Practice Guide*, 77 Fed. Reg. 48,756, 48,766 (Aug. 14, 2012).

Under the broadest reasonable construction standard, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). "Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004). "Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Claims 1 and 6 recite methods of treating a human patient with Pompe's disease having the step of intravenously administering biweekly to the patient a therapeutically effective amount of human acid alpha glucosidase. Petitioner sets forth what it considers to be the ordinary meaning for claim terms: "human acid alpha glucosidase," "therapeutically effective amount," and "biweekly." Pet. 29-33. Patent Owner does not challenge Petitioner's proposed claim construction. Petitioner's proposed constructions are reasonable at this stage of the proceeding. We therefore adopt them for the purposes of this decision.

The claim 1 feature of "whereby the concentration of accumulated glycogen in the patient is reduced and/or further accumulation of glycogen is arrested" is not a separate step, but rather a result of administering a therapeutically effective

amount of human acid alpha glucosidase according to the claimed method. Such results are not generally considered a patentable feature separate from the expressly recited steps of the claimed method. *See*, *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc*., 246 F.3d 1368, 1376 (Fed. Cir. 2001) (recognizing that "[n]ewly discovered results of known processes directed to the same purpose are not patentable."); *see also, Abbott Labs. v. Baxter Pharm. Products, Inc*., 471 F.3d 1363, 1369 (Fed. Cir. 2006). Accordingly, we do not consider the phrase "the concentration of accumulated glycogen in the patient is reduced and/or further accumulation of glycogen is arrested" to further limit the phrase "a therapeutically effective amount of human acid alpha glucosidase." Pet. 32.

Similarly, the claim 6 feature of "whereby hypertrophic cardiomyopathy in the patient is reduced and/or arrested" is not a separate step, but rather a result of administering a therapeutically effective amount of human acid alpha glucosidase according to the claimed method. Such results are not generally considered a separate patentable feature. *Id.* Accordingly, we do not consider the phrase "whereby hypertrophic cardiomyopathy in the patient is reduced and/or arrested" to further limit the phrase "a therapeutically effective amount of human acid alpha glucosidase."

B. Asserted Grounds of Unpatentability

1. Anticipation of Claims 1 and 3 by Duke Press Release 1997

Petitioner contends that claims 1 and 3 are fully anticipated by Duke Press Release 1997. Pet. 34-40. Patent Owner contends that Duke Press Release 1997 (Ex. 1002) does not disclose "human acid alpha glucosidase" and thus cannot anticipate the claims. Prelim. Resp. 2.

Upon review of Petitioner's analysis and supporting evidence, we determine

that Petitioner has not shown a reasonable likelihood of prevailing on its assertion that claims 1 and 3 are anticipated by Duke Press Release 1997. The Duke Press Release 1997 details an FDA clinical trial study in which infants with Pompe's disease were injected with recombinant acid alpha glucosidase in order to evaluate the safety and efficacy of the recombinant enzyme treatment. Ex. 1002; Pet. 31-32. The press release states that the trial will test "recombinant enzyme" therapy, however, the enzyme is not identified as "human" enzyme as required by claims 1 and 3. Thus, human acid alpha glucosidase is not expressly disclosed. Petitioner makes no assertion that the acid alpha glucosidase disclosed by Duke Press Release 1997 is inherently disclosed. Petitioner, therefore, has not demonstrated a reasonable likelihood that Duke Press Release 1997 discloses human acid alpha glucosidase as required by the claims.

2. Obviousness of Claims 1 and 3 over the Combination of Duke Press Release 1997, Reuser, and Van Hove

Petitioner contends that claims 1 and 3 are obvious over the combination of Duke Press Release 1997, Reuser, and Van Hove. Pet. 49-51. Upon review of Petitioner's analysis and supporting evidence, we determine that Petitioner has demonstrated that there is a reasonable likelihood that it would prevail on the ground that claims 1 and 3 would have been obvious over Duke Press Release 1997, Reuser, and Van Hove.

The Duke Press Release 1997 details an FDA clinical trial study in which infants with Pompe's disease were injected with recombinant acid alpha glucosidase in order to evaluate the safety and efficacy of the recombinant enzyme treatment. Ex. 1002; Pet. 31-32. The Duke Press Release 1997 does not disclose the dosing regimen or route of administration used for the study and thus does not expressly disclose the feature of "intravenously administering biweekly" as recited

in claim 6. Further, as discussed above, Duke Press Release 1997 also does not disclose using "human" acid alpha glucosidase.

Reuser, however, discloses the production of human acid alpha glucosidase for use in enzyme replacement therapy to treat Pompe's disease. Ex. 1005, 2-3 and 21-23 (Example 1); Pet. 41-42. Reuser discloses intravenous administration "in an amount sufficient to reduce the concentration of accumulated metabolite and/or prevent or arrest further accumulation of metabolite." *Id.* at 20, ll. 9-28. In the case of Pompe's disease, glycogen is the metabolite. *Id.* at 2. Reuser further describes a "therapeutically effective dose" as being dependent on the condition and general state of the patient's health. *Id. at* 20, ll. 25-28.

With regard to claim 3, Reuser specifies that the recognized species of acid alpha glucosidase includes the 110/100 kDa precursor. *Id.* at 9. Additionally, Petitioner relies on Van Hove to show the purification of human acid alpha glucosidase using the 110 kDa form for the purposes of enzyme replacement therapy in Pompe's disease. Ex. 1012, 613.

The above evidence reasonably supports the Petitioner's position that the method of treating a human patient with Pompe's disease comprising administering intravenously to the patient a therapeutically effective amount of human acid alpha glucosidase as required by claims 1 and 3 would have been obvious to a person of ordinary skill in the art. We, therefore, conclude that there is a reasonable likelihood that Petitioner will prevail in proving obviousness of claims 1 and 3 over the combination of Duke Press Release 1997, Reuser, and Van Hove.

3. Obviousness of Claims 4-6 over the Combination of Duke Press Release 1997, Reuser, Barton, and Van der Ploeg

Upon review of Petitioner's analysis and supporting evidence, we determine

that Petitioner has demonstrated that there is a reasonable likelihood that it would prevail on the ground that claims 4-6 would have been obvious over Duke Press Release 1997, Reuser, Barton, and Van der Ploeg.

a. Claims 4 and 6

Claim 4 depends directly from claim 1 and requires weekly administration of acid alpha glucosidase. Independent claim 6 differs from claim 1, *inter alia*, in that the method claim 6 requires biweekly administration of the enzyme. Petitioner further relies on Barton (Ex. 1004) and Van der Ploeg (Ex. 1032) to reach these elements of claims 4 and 6.

Barton discloses a biweekly intravenous administration schedule for enzyme replacement therapy (*i.e.*, biweekly intravenous administration of glucocerebrosidase to patients with Gaucher's Disease). Van der Ploeg discloses a tissue half-life of acid alpha glucosidase of 6-9 days (Ex. 1032, 91, right col., final ¶). Petitioner further relies on the Declaration of Dr. Pastores as evidence that a clinician would have chosen the biweekly dosing schedule based on this half-life, or a weekly dosing schedule should the severity of the disease call for more frequent dosing (Ex. 1030, ¶¶ [0086]-[0090]). Moreover, Barton discloses weekly dosing in severe cases. Ex. 1004, 1465, left col., 2nd full ¶.

The above evidence reasonably supports the Petitioner's position that it would have been obvious to select a weekly or biweekly intravenous administration for the purposes of initially determining the clinical effectiveness of the enzyme replacement therapy disclosed in the Duke Press Release 1997. *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 417 (2007) ("If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability."); *see also, In re Boesch*, 617 F.2d 272, 276 (CCPA 1980) ("[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill

of the art." (Citations omitted)).

For those reasons, we conclude that there is a reasonable likelihood that Petitioner will prevail in demonstrating that claims 4 and 6 are rendered obvious by the combination of Duke Press Release 1997, Reuser, Barton, and Van der Ploeg.

b. Claim 5

Claim 5 requires that the therapeutically effective amount of human acid alpha glucosidase is at least 10 mg/kg body weight of the patient. Petitioner relies on Reuser to meet that limitation, as Reuser discloses a dosage range from 0.1 to 10 mg/kg of purified enzyme per kilogram of body weight. Pet. 47, citing Ex. 1005, p. 20, ll. 27-28. That disclosure in Reuser provides a sufficient reason to combine the prior art references and supports a conclusion of obviousness. *Galderma Labs., L.P. v. Tolmar, Inc*., 737 F.3d 731, 738 (Fed. Cir. 2013)

> [W]here there is a range disclosed in the prior art, and the claimed invention falls within that range, the burden of production falls upon the patentee to come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations.

Citing *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd*., 719 F.3d 1346, 1352-54 (Fed. Cir. 2013).

For those reasons, we conclude that there is a reasonable likelihood that Petitioner will prevail in demonstrating that claim 5 is rendered obvious by the combination of Duke Press Release 1997, Reuser, Barton, and Van der Ploeg.

4. Redundant Grounds

Petitioner also asserts that claims 1 and 3 are obvious over the combination of Duke Press Release 1997 and Reuser. Pet. 41-44. Petitioner makes no meaningful distinction between these grounds and the grounds on which the Board

has already granted the Petition to institute *inter partes* review. Petitioner's remaining grounds, therefore, are denied as redundant. 37 C.F.R. § 42.108(a).

III. CONCLUSION

Petitioner has not demonstrated a reasonable likelihood of prevailing on its challenge of claims 1 and 3 as anticipated by Duke Press Release 1997.

Petitioner has demonstrated a reasonable likelihood of prevailing on its challenge of claims 1 and 3 of the '226 patent under 35 U.S.C. § 103 as obvious over the combination of Duke Press Release 1997, Reuser, and Van Hove.

Petitioner has demonstrated a reasonable likelihood of prevailing on its challenge of claims 4-6 of the '226 patent under 35 U.S.C. § 103 as obvious over the combination of Duke Press Release 1997, Reuser, Barton and Van der Ploeg.

Petitioner's other challenges are denied as redundant to the above challenges.

IV. ORDER

For the reasons given, it is

ORDERED that the Petition is *granted* as to claims 1 and 3-6 of the '226 patent with respect to the following alleged grounds:

1. Claims 1 and 3 of the '226 patent under 35 U.S.C. § 103 as obvious over the combination of Duke Press Release 1997, Reuser, and Van Hove;
2. Claims 4-6 of the '226 patent under 35 U.S.C. § 103 as obvious over the combination of Duke Press Release 1997, Reuser, Barton and Van der Ploeg.

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(a), *inter partes* review of the '226 patent is hereby instituted commencing 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;

FURTHER ORDERED that all other grounds presented in the Petition are *denied*, and no ground other than those specifically granted above is authorized for the *inter partes* review as to claims 1-6 of the ’226 patent; and

FURTHER ORDERED that an initial conference call with the Board is scheduled for 2 PM Eastern Time on March 17, 2014. The parties are directed to the Office Trial Practice Guide, 77 Fed. Reg. 48756, 48765-66 (Aug. 14, 2012) for guidance in preparing for the initial conference call, and should come prepared to discuss any proposed changes to the Scheduling Order entered herewith and any motions the parties anticipate filing during the trial.

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