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Paper 53
Entered: November 3, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PAR PHARMACEUTICAL, INC.,
LUPIN LTD., and LUPIN PHARMACEUTICALS, INC.,

Petitioners,

v.

HORIZON THERAPEUTICS, LLC,[1]
Patent Owner.

Case IPR2015-01117[2]
Patent 8,642,012 B2

Before TONI R. SCHEINER, DEBORAH KATZ, and
GRACE KARAFFA OBERMANN, *Administrative Patent Judges*.

SCHEINER, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318 and 37 C.F.R. § 42.73

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[1] Patent owner represents "that it has changed name and converted form and is now Horizon Therapeutics, LLC." Paper 51.

[2] Case IPR2016-00283, instituted on a petition filed by Lupin Ltd. and Lupin Pharmaceuticals, Inc., has been joined with Case IPR2015-01117. *See* Paper 32.

I. INTRODUCTION

Par Pharmaceutical, Inc. ("Par" or "Petitioner Par") filed a Petition (Paper 2, "Pet.") on April 29, 2015, requesting an *inter partes* review of claims 1–12 of U.S. Patent No. 8,642,012 B2 (Ex. 1001, "the '012 patent"). Horizon Therapeutics, Inc. ("Horizon" or "Patent Owner") filed a Preliminary Response (Paper 8) on August 5, 2015. On November 4, 2015, we instituted trial as to all of the challenged claims, on the following grounds.[3]

References	**Basis**	**Claims Challenged**
Brusilow '91,[4] Sherwin '19,[5] Comte,[6] and Shiple[7]	§ 103	1, 3, 4, 7, 8, 10, 12

[3] Par supported its challenge with a Declaration, executed April 29, 2015, by Neal Sondheimer, M.D., Ph.D. ("Sondheimer Declaration") (Ex. 1002).

[4] Saul W. Brusilow, *Phenylacetylglutamine May Replace Urea as a Vehicle for Waste Nitrogen Excretion*, 29 PEDIATRIC RESEARCH 147–150 (1991) ("Brusilow '91") (Ex. 1012).

[5] Carl P. Sherwin at al., *The Maximum Production of Glutamine by the Human Body as Measured by the Output of Phenylacetylglutamine*, 37 J. BIOL. CHEM. 113–119 (1919) ("Sherwin '19") (Ex. 1016).

[6] Blandine Comte et al., *Identification of phenylbutyrylglutamine, a new metabolite of phenylbutyrate metabolism in humans*, 37 J. MASS SPECTROM. 581–590 (2002) ("Comte") (Ex. 1025).

[7] George J. Shiple & Carl P. Sherwin, *Synthesis of Amino Acids in Animal Organisms. I. Synthesis of Glycocoll and Glutamine in the Human Organism*, 44 J. AMER. CHEM. SOC. 618–624 (1922) ("Shiple") (Ex. 1017).

References	Basis	Claims Challenged
Brusilow '91 , Sherwin '19, Shiple, and Fernandes[8]	§ 103	5
Brusilow '91, Sherwin '19, Shiple, and the '647 patent[9]	§ 103	2, 9
Brusilow '91, Sherwin '19, Shiple, Kasumov,[10] and the '979 patent[11]	§ 103	6, 11

After institution, Lupin Ltd. and Lupin Pharmaceuticals, Inc. ("Lupin") filed a Petition based on the same grounds as the Par Petition, with arguments and evidence substantially identical to those put forth by Par. *See* IPR2016-00283, Paper 1. Lupin's Petition was accompanied by a Motion for Joinder. *See* IPR2016-00283, Paper 4. We instituted trial on the same challenges of Lupin's Petition that we instituted trial on in the current *inter partes* review and joined the two proceedings in this single review. No

[8] INBORN METABOLIC DISEASES: DIAGNOSIS AND TREATMENT 219–220 (John Fernandes et al. eds., Springer Verlag 3d ed. 2000) ("Fernandes") (Ex. 1011).

[9] U.S. Patent No. 4,284,647, issued August 18, 1981 to Brusilow et al. ("the '647 patent") (Ex. 1018).

[10] Takhar Kasumov et al., *New Secondary Metabolites of Phenylbutyrate in Humans and Rats*, 32 DRUG METABOLISM AND DISPOSITION 10–19 (2004) ("Kasumov") (Ex. 1015).

[11] U.S. Patent No. 5,968,979, issued October 19, 1999 to Brusilow ("the '979 patent") (Ex. 1026).

further submissions have been entered on Lupin's part. Paper 32; *see* IPR2016-00283, Paper 12.

Horizon filed a Patent Owner Response (Paper 25, "PO Resp."), and Par filed a Reply (Paper 30, "Reply"). With our authorization, Horizon filed a Corrected Patent Owner Response (Paper 41, "Corr. PO Resp.")—superseding Paper 25—in order to correct citations to Exhibit 2012. *See* Paper 40. Petitioner Par, with our authorization, filed a Supplemental Reply to the Corrected Patent Owner Response (Paper 45, "Supp. Reply"). Horizon did not move to amend any claim of the '012 Patent.

Horizon and Par each filed a Motion to Exclude (Papers 36, 38), and each filed an Opposition to the Motion of the other party (Papers 42, 44). In addition, Horizon filed a Reply to Par's Opposition (Papers 46).

We heard oral argument on July 26, 2016. A transcript of the argument has been entered into the record as Paper 52.

We have jurisdiction under 35 U.S.C. § 6. Petitioner bears the burden of proving unpatentability of the challenged claims, and that burden never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, Petitioner must establish facts supporting its challenge by a preponderance of the evidence. *See* 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

For the reasons that follow, we determine that Par has not proved by a preponderance of the evidence that claims 1–12 are unpatentable.

A. Related Proceedings

Patent Owner filed suit against Petitioner, alleging infringement of the '012 patent and U.S. Patent No. 8,404,215 B1 ("the '215 patent) in *Hyperion Therapeutics, Inc. v. Par Pharmaceutical, Inc.*, Case No. 2:14-CV-384-JRG-RSP (E.D. Tex.). Pet. 7; Paper 5, 3. In addition, concurrently with the Petition under consideration here, Petitioner Par filed a petition challenging the claims of the '215 patent (IPR2015-01127), but represents that that patent is not related to the '012 patent. Pet. 7.

In addition, Patent Owner filed suit against Lupin, alleging infringement of the '012 patent, in *Horizon Therapeutics, Inc. v. Lupin Ltd.*, Case No. 1:15-cv-07624-RBK-JS (D.N.J. filed Oct. 19, 2015). *See* IPR2016-00283, Paper 1, 8.

B. The '012 Patent (Ex. 1001)

The '012 patent, titled "Methods of Treatment Using Ammonia-Scavenging Drugs," is directed to "treatment of patients with nitrogen retention states, in particular urea cycle disorders (UCDs) . . . [by] administer[ing] compounds that assist in elimination of waste nitrogen from the body." Ex. 1001, 1:18–25. These compounds—or "nitrogen scavenging drugs"[12]—include glyceryl tri-[4-phenylbutyrate] (HPN-100) and phenylbutyric acid (PBA)—both of which are prodrugs that are converted *in vivo* to phenylacetic acid (PAA). *Id.* at 3:61–66.

[12] The terms "ammonia scavenger" and "nitrogen scavenger" are used interchangeably in the '012 patent. Ex. 1001, 4:6–7.

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