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Paper 34
Date: November 13, 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MALLINCKRODT PHARMACEUTICALS IRELAND LIMITED,
Petitioner,

v.

BIOVIE, INC.,
Patent Owner.

IPR2018-00974
Patent 9,655,945 B2

Before ERICA A. FRANKLIN, MICHELLE N. ANKENBRAND, and KRISTI L. R. SAWERT, *Administrative Patent Judges.*

SAWERT, *Administrative Patent Judge*.

JUDGMENT

Final Written Decision
Determining All Challenged Claims Unpatentable
Denying Patent Owner's Motion to Amend
35 U.S.C. § 318(a)

Granting-In-Part Petitioner's Motion to Strike
37 C.F.R. § 42.5

I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review challenging the patentability of claims 1–14 ("the challenged claims") of U.S. Patent No. 9,655,945 B2 ("the '945 patent," Ex. 1001). We have jurisdiction under 35 U.S.C. § 6, and enter this Decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons set forth below, we determine that Petitioner has shown, by a preponderance of the evidence, that the challenged claims are unpatentable. *See* 35 U.S.C. § 316(e) (2012). Additionally, we deny Patent Owner's contingent Motion to Amend, and grant-in-part Petitioner's Motion to Strike.

A. Procedural History

Mallinckrodt Pharmaceuticals Ireland Limited ("Petitioner") filed a Petition for an *inter partes* review under 35 U.S.C. § 311. Paper 2 ("Pet."). Petitioner supported its Petition with the Declaration of Dr. Paul Gow. Ex. 1002. BioVie, Inc. ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp.").

On November 14, 2018, pursuant to 35 U.S.C. § 314(a), we instituted trial to determine whether any challenged claim of the '945 patent is unpatentable based on the grounds raised in the Petition:

Claims Challenged	35 U.S.C. §	Reference(s)
1–3, 5	102	Robertson[1]
7, 8, 10	103	Robertson

[1] Marcus Robertson et al., *Continuous Outpatient Terlipressin Infusion for Hepatorenal Syndrome as a Bridge to Successful Liver Transplantation*, HEPATOLOGY 2125–26 (Dec. 2014) ("Robertson," Ex. 1004).

Claims Challenged	35 U.S.C. §	Reference(s)
1, 2, 6, 12	103	Angeli[2]
1–14	103	Fimiani,[3] Robertson
1–14	103	Fimiani, Angeli

Paper 9, 6, 31 ("Institution Decision" or "Inst. Dec.").

Patent Owner filed a Response. Paper 15 ("PO Resp."). Patent Owner supported its Response with the Declaration of Dr. Jaime Bosch. Ex. 2023. Patent Owner also filed a contingent Motion to Amend. Paper 16 ("Motion to Amend" or "Mot. Amend."). Petitioner filed a Reply to Patent Owner's Response (Paper 18, "Pet. Reply"), and an Opposition to Patent Owner's Motion to Amend (Paper 19, "Opp. Mot. Amend."). Patent Owner filed a Sur-reply (Paper 21, "PO Sur-reply"), and a Reply in support of its Motion to Amend (Paper 22, "Reply Mot. Amend."). Patent Owner's Sur-reply was accompanied by a Supplemental Declaration of Dr. Bosch. Ex. 2044. Petitioner filed a Sur-reply to Patent Owner's Reply. Paper 25 ("Sur-reply Mot. Amend.").

On our authorization (Paper 26), Petitioner filed a Motion to Strike (Paper 28, "Mot. Strike"), to which Patent Owner filed an Opposition (Paper 29, "Opp. Mot. Strike").

An oral hearing was held on August 12, 2019. A transcript of the hearing is included in the record. Paper 30 ("Tr."). After the hearing, and

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[2] Paolo Angeli, *Terlipressin for the treatment of hepatorenal syndrome in patients with cirrhosis*, 1 EXPERT OPIN. ORPHAN DRUGS 241–48 (2013) ("Angeli," Ex. 1005).

[3] Basilio Fimiani et al., *The use of terlipressin in cirrhotic patients with refractory ascites and normal renal function: A multicentric study*, 22 EUR. J. INTERN. MED. 587–90 (2011) ("Fimiani," Ex. 1006).

on our authorization (Paper 31), Patent Owner filed a Notice of Supplemental Authority (Paper 32, "PO Notice"), to which Petitioner filed a Reply (Paper 33, "Pet. Reply to Notice").

B. Real Parties in Interest

Petitioner identifies its real parties-in-interest as Mallinckrodt Pharmaceuticals Ireland Limited and Mallinckrodt Hospital Products Inc. Pet. 3. Patent Owner identifies its real party-in-interest as BIOVIE, Inc. Paper 4, 2.

C. Related Matters

According to the parties, there are no pending judicial proceedings involving the '945 patent. Pet. 3; Paper 4, 2. Petitioner states that U.S. Patent Application No. 15/491,613 is related to the '945 patent and is currently pending before the Office. Pet. 3.

D. The '945 Patent

The '945 patent, titled "Treatment of Ascites," issued on May 23, 2017. Ex. 1001, code (45). The '945 patent relates to "a method for treating ascites patients by administering the peptide drug terlipressin." *Id.* at 1:14–15.

According to the '945 patent, "[a]scites is a frequent and life-threatening complication of advanced liver cirrhosis with an expected 40% mortality rate within two years of diagnosis." *Id.* at 1:18–20. Although there is no FDA-approved drug for treating ascites, diuretics are administered off-label "with limited and temporary efficacy." *Id.* at 1:20–23. As liver cirrhosis progresses, however, a patient's ascites may become refractory (i.e., unmanageable) with diuretics. *Id.* at 1:26–28.

Patients suffering from refractory ascites may also develop hepatorenal syndrome (HRS)—another complication of advanced liver cirrhosis that marks the beginning of renal failure. *Id.* at 2:26–28. There are two types of HRS: type 1 (HRS-1) and type 2 (HRS-2). *Id.* at 2:43–46. HRS-1 is more severe than HRS-2, and thus, HRS-1 patients require hospitalization, whereas HRS-2 patients are ambulatory. *Id.* at 2:42–45.

The '945 patent states that HRS-1 patients have been successfully treated with intravenous (IV) injections of terlipressin every 4 to 6 hours. *See id.* at 1:23–26 (stating that terlipressin has been used to "save their lives"). The '945 patent also states, "investigational studies have shown that IV injections of terlipressin every 4 to 6 hours in combination with diuretics may resolve refractory ascites in hospitalized patients and decrease the need for large volume paracentesis (ascites fluid withdrawal by needle)." *Id.* at 1:28–33. These high-dose IV injections, however, "carry a high risk of side effects." *Id.* at 1:33–34. The '945 patent states that "[m]ore recent studies with hospitalized HRS patients indicate that a continuous infusion of terlipressin can achieve similar efficacy to intermittent injections with a much better safety profile." *Id.* at 1:34–37. But "to date there have been no published studies of using a continuous low-dose infusion terlipressin to manage ascites in non-hospitalized patients with cirrhosis." *Id.* at 1:37–40.

The '945 patent states that the present inventors "have identified a need in the art for a method to treat ascites patients on an outpatient basis and potentially avoid or delay the need for hospitalization due to HRS or other life-threatening complications." *Id.* at 1:41–44. In one embodiment, terlipressin may be administered continuously by a pump at a dosage range of about 0.5 gm to about 20 mg every 24 hours, for a period from about one

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