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Paper 39
Entered: August 2, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LUPIN LIMITED,
Petitioner,

v.

VERTEX PHARMACEUTICALS INCORPORATED,
Patent Owner.

Case IPR2016-00558
Patent 6,436,989 B1

Before LORA M. GREEN, SHERIDAN K. SNEDDEN, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

SNEDDEN, Administrative Patent Judge.

FINAL WRITTEN DECISION
Determining Claims 2, 3, and 10–12 Not Shown to be Unpatentable
35 U.S.C. § 318(a); 37 C.F.R. § 42.73

I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review challenging the patentability of claims 2, 3, and 10–12 (collectively, "the challenged claims") of U.S. Patent No. 6,436,989 B1 (Ex. 1001; "the '989 Patent"). We have jurisdiction under 35 U.S.C. § 6. For the reasons that follow, we determine that Petitioner failed to demonstrate, by a preponderance of evidence, that claims 2, 3, and 10–12 are unpatentable.

A. Procedural History

Lupin Limited ("Petitioner") filed a Petition (Paper 1; "Pet.") to institute an *inter partes* review of claims 2, 3, and 10–12 of the '989 Patent. Vertex Pharmaceuticals Incorporated ("Patent Owner") filed a Patent Owner Preliminary Response. Paper 8 ("Prelim. Resp."). Based on these submissions, we instituted trial on the following grounds of unpatentability asserted by Petitioners:

Reference[s]	Basis	Claims challenged
Roy[1] and Grobelny[2]	§ 103(a)	2
Roy, Grobelny, and Bighley[3]	§ 103(a)	3, 10–12

Decision to Institute (Paper 9, "Dec.").

[1] Ex. 1021, U.S. Patent No. 6,730,679 B1, issued May 4, 2004 to Roy et al. (hereinafter "Roy" or "the '679 Patent").

[2] Ex. 1022, International Patent Application Publication Number WO 95/07269, published March 16, 1995, and naming Damian Grobelny as the sole inventor (hereinafter "Grobelny" or "the '269 Publication").

[3] Ex. 1027, Bighley, et al., *Salt Forms of Drugs and Absorption*, *in* 13 ENCYCLOPEDIA OF PHARMACEUTICAL TECHNOLOGY 453–499 (James Swarbrick & James C. Boylan eds. 1996) (hereinafter "Bighley").

After institution of trial, Patent Owner filed a Patent Owner Response (Paper 13, "PO Resp."), to which Petitioners filed a Reply (Paper 24, "Reply").

Petitioners rely on the Declarations of Jed Fisher (Ex. 1002 and Ex. 1096) in support of the proposed grounds of unpatentability.

Patent Owner relies on the Declaration of Richard Ogden, Ph.D. (Ex. 2017).

Patent Owner filed a motion to exclude certain of Petitioners' evidence. Paper 27. Petitioners filed an opposition (Paper 29), and Patent Owner filed a reply (Paper 30).

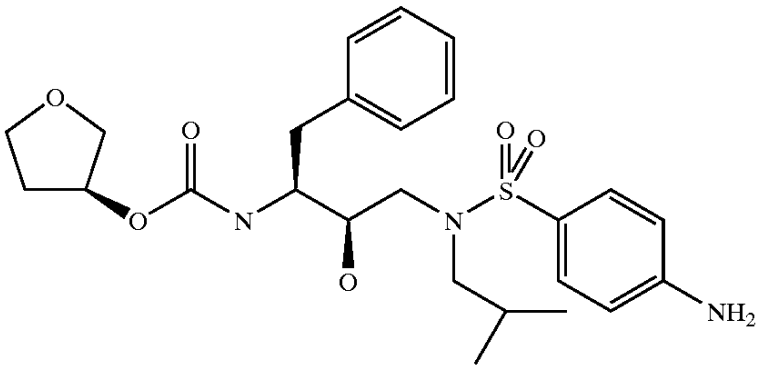
Oral argument was conducted on April 5, 2017. A transcript is entered as Paper 38 ("Tr.").

B. The '989 Patent (Ex. 1001)

The '989 patent is directed to prodrugs of HIV aspartyl protease inhibitors, pharmaceutical compositions thereof, and methods of treating mammals therewith. Ex. 1001, 1:5–17. Prodrugs generally are inactive compounds that convert to an active form in the body. *Id.* at 2:7–16, 33:25–34. Usually, a prodrug has some improved pharmacological property over the active drug, such as improved stability or solubility. *Id.* The prodrugs of the '989 patent are said to have favorable aqueous solubility, to have high oral bioavailability and facile in vivo generation of the active ingredient, and to be particularly well suited for decreasing pill burden and increasing patient compliance. *Id.* at 1:6–15.

The relevant compound of the '989 patent is a prodrug of the known HIV aspartyl protease inhibitor, VX-478 (4-amino-N-((2-syn, 3S)-2-hydroxy-4-phenyl-2((S)-tetrahydrofuran-3-yl-oxycarbonylamino)butyl-N-

isobutyl-benzenesulfonamide), also known as amprenavir. *Id.* at 1:30–42, 30:29–34:67; Prelim. Resp. 18; Ex. 1002, ¶ 20, n.1. Amprenavir has the following structure:



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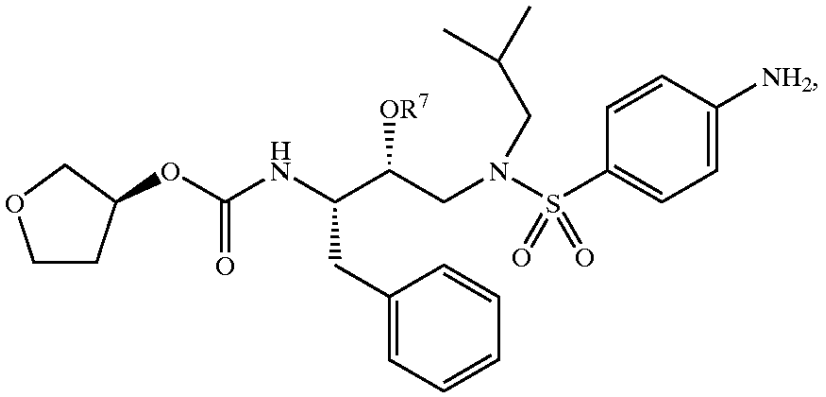
Ex. 1001, 30:32–31:5.

Examples 27 to 30 detail the process for forming phosphate ester derived prodrugs of amprenavir. *Id.* at 57:1–60:14. Example 30, in particular, describes a disodium phosphate ester salt prodrug of amprenavir. *Id.* at 59:9–20, 60:1–21.

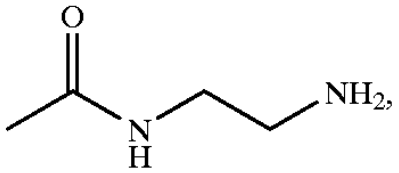
C. Challenged Claims

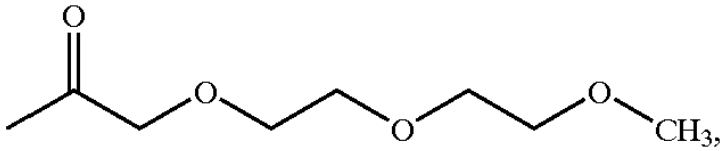
The challenged "claims cover the drug Lexiva® (fosamprenavir calcium), which is marketed for the treatment of human immunodeficiency virus-1 ('HIV')." PO Resp. 1; *see* Pet. 4–5. Challenged claims 2 and 3 depend from claim 1 of the '989 patent. Challenged claims 10–12 depend from claim 4 of the '989 patent. Claims 1–4 and 10–12 of the '989 patent are reproduced below:

1. A compound of the formula:

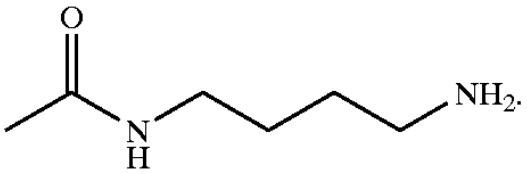


wherein: R^7 is selected from $-PO_3^{2-}Na_2^+$, $-PO_3^{2-}K_2^+$, $-PO_3^{2-}Mg^{2+}$, $-PO_3^{2-}Ca^{2+}$,





or



2. The compound according to claim 1, wherein:

R^7 is selected from —$PO_3^{2-}Na_2^+$, —$PO_3^{2-}K_2^+$, or —$PO_3^{2-}Ca^{2+}$.

3. The compound according to claim 2, wherein R^7 is — $PO_3^{2-}Ca^{2+}$.

4. A pharmaceutical composition, comprising a compound according to any one of claims 1 to 3 in an amount effective to treat infection by a virus that is characterized by a virally-encoded aspartyl protease; and a pharmaceutically acceptable carrier, adjuvant or vehicle.

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