United States Court of Appeals for the Federal Circuit

NOVARTIS AG, MITSUBISHI PHARMA CORP.,
Appellants

v.

TORRENT PHARMACEUTICALS LIMITED, APOTEX INC., MYLAN PHARMACEUTICALS INC.,
Appellees

2016-1352

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2014-00784, IPR2015-00518.

Decided: April 12, 2017

ROBERT TRENCHARD, Gibson, Dunn & Crutcher LLP, New York, NY, argued for appellants. Appellant Novartis AG also represented by JANE M. LOVE; MICHAEL A. VALEK, Dallas, TX; ALEXANDER N. HARRIS, San Francisco, CA.

JOSEPH M. O'MALLEY, JR., Paul Hastings LLP, New York, NY, for appellant Mitsubishi Pharma Corp. Also represented by ERIC WILLIAM DITTMANN.

TERESA STANEK REA, Crowell & Moring, LLP, Washington, DC, argued for appellees. Appellee Apotex Inc. also represented by VINCENT JOHN GALLUZZO; JONATHAN M. LINDSAY, Irvine, CA.

MICHAEL K. LEVY, Andrews Kurth Kenyon LLP, New York, NY, for appellee Torrent Pharmaceuticals Limited.

SHANNON BLOODWORTH, Perkins Coie, LLP, Washington, DC, for appellee Mylan Pharmaceuticals Inc. Also represented by BRANDON MICHAEL WHITE; DAN L. BAGATELL, Hanover, NH.

Before TARANTO, CHEN, and STOLL, *Circuit Judges*.

CHEN, *Circuit Judge*.

This is an appeal from the Final Written Decision of the United States Patent and Trademark Office, Patent Trial and Appeal Board (Board) in two consolidated *inter partes* review (IPR) proceedings of U.S. Patent No. 8,324,283 (the '283 patent), owned by Novartis AG and Mistubishi Tanabe Pharma Corp. (collectively, Novartis). The Board instituted IPRs on all claims of the '283 patent based on petitions filed by Torrent Pharmaceuticals Limited, Apotex, Inc. and Mylan Pharmaceuticals Inc. (collectively, Petitioners). After reviewing the claims, receiving extensive briefing, and hearing oral argument, the Board found all original claims of the '283 patent and Novartis' proposed substitute claims unpatentable as obvious. *See Torrent Pharm. Ltd. v. Novartis AG*, Nos. IPR2014-00784, IPR2015-00518, 2015 WL 5719630 (PTAB Sept. 24, 2015) (*Final Written Decision*). Novartis raises a series of challenges to the Board's analysis of the evidence and ultimate determination of unpatentability. For the reasons stated below, we *affirm*.

BACKGROUND

I.

The '283 patent relates to a solid pharmaceutical composition suitable for oral administration, comprising a sphingosine-1 phosphate (S1P) receptor agonist and a sugar alcohol, which the patent explains is useful for the treatment of certain autoimmune diseases such as multiple sclerosis. '283 patent, col. 1, lines 11–14, 33–35; col. 12, lines 19–49. According to the specification, S1P receptor agonists generally exhibit properties that make formulations suitable for oral administration of a solid composition difficult to create. However, "solid compositions comprising a sugar alcohol provide formulations which are particularly well suited to the oral administration of S1P receptor agonists." *See id.* at col. 1, lines 36–39. They also "provide a convenient means of systemic administration of S1P receptor agonists, do not suffer from the disadvantages of liquid formulations for injection or oral use, and have good physiocochemical and storage properties." *Id.* at col. 1, lines 39–43. In such a composition, the S1P receptor agonist is the active ingredient and the sugar alcohol acts as an excipient—the substance formulated alongside the active ingredient as a diluent, carrier, filler and/or bulking agent for the composition. *See id.* at col. 9, lines 53–54.

The '283 patent states that there are multiple known S1P receptor agonists appropriate for use in the claimed invention, set forth in the specification as formulas I–XIII. *Id.* at col. 1, line 51 to col. 8, line 4. The '283 patent also states that a "particularly preferred S1P receptor agonist of formula I is FTY720, i.e., 2-amino-2-[2-(4-octylphenyl) ethyl]propane-1,3-diol in free form or in a pharmaceutically acceptable salt form . . . ." *Id.* at col. 8, lines 23–26. FTY720 is also known as fingolimod. The '283 patent further discloses that the specific sugar alcohol used in the claimed composition "may suitably be mannitol,"

because of its non-hygroscopic properties (i.e., it is not likely to absorb moisture, which is beneficial in manufacturing solid oral pills). *Id.* at col. 9, lines 53–54.

Claims 1 and 19 of the '283 patent are the only independent claims and are illustrative of the claimed subject matter:

> 1. A solid pharmaceutical composition suitable for oral administration, comprising:
>
> > (a) a S1P receptor agonist which is selected from 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, 2-amino-2-[4-(3-benzyloxyphenoxy)-2-chlorophenyl]propyl-1,3-propane-diol, 2-amino-2-[4-(3-benzyloxyphenylthio)-2-chlorophenyl]propyl-1,3-propane-diol, or 2-amino-2-[4-(3-benzyloxyphenylthio)-2-chlorophenyl]-2-ethyl-1,3-propane-diol, and its phosphates or a pharmaceutically acceptable salt thereof; and
> >
> > (b) a sugar alcohol.
>
> 19. A solid pharmaceutical composition suitable for oral administration, comprising mannitol and 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol or a pharmaceutically acceptable salt thereof.

Id. at col. 17, lines 2–11; col. 18, lines 7–10. Thus, claim 1 is directed towards a solid oral composition comprised of the combination of one of a handful of S1P receptor agonists and any sugar alcohol, whereas claim 19 is directed towards the specific combination of fingolimod and mannitol in a solid oral composition.

The dependent claims are directed towards various refinements of the composition, including for example, the addition of a lubricant:

> 20. A composition according to claim 19, further comprising a lubricant.

Id. at col. 18, lines 11–12. Other claims are directed towards adjusting the respective amount of ingredients:

> 22. A composition according to claim 19, wherein the compound 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, or a pharmaceutically acceptable salt thereof, is present in an amount of 0.5 to 5% by weight, based on the total weight of the composition.
>
> 23. A composition according to claim 19, wherein mannitol is present in an amount of 90 to 99.5% by weight, based on the total weight of the composition.

Id. at col. 18, lines 15–22.

While the application leading to the '283 patent was pending at the Patent Office, Novartis applied to the U.S. Food and Drug Administration (FDA) for approval to sell a fingolimod-mannitol pill to treat multiple sclerosis under the "Gilenya" brand name. The FDA approved Gilenya for the treatment of multiple sclerosis in 2010.

II.

On May 27, 2014, Torrent filed a petition to institute an *inter partes* review of claims 1–32 of the '283 patent. Torrent's petition presented three separate patentability challenges:

> 1. claims 1–32 are unpatentable as obvious over the combination of U.S. Patent No. 6,004,565 (Chiba) and *Pharmaceutics: The Science of Dosage Form Design* (Aulton); and
>
> 2. claims 1–4, 7, 8, 19, 22 and 32 are unpatentable as anticipated by U.S. Patent No. 6,277,888 (Sakai); and

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