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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

ASTRAZENECA AB,
Patent Owner.

Case IPR2016-01325
Patent 8,329,680 B2

Before BRIAN P. MURPHY, ZHENYU YANG, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

POLLOCK, *Administrative Patent Judge*.

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

I. INTRODUCTION

Mylan Pharmaceuticals, Inc. ("Petitioner")[1] filed a Petition requesting an *inter partes* review of claims 1–20 of U.S. Patent No. 8,329,680 B2 (Ex. 1001, "the '680 Patent"). Paper 2 ("Pet."). AstraZeneca AB ("Patent Owner") filed a Preliminary Response to the Petition. Paper 10 ("Prelim. Resp."). We have jurisdiction under 35 U.S.C. § 6 and 35 C.F.R. § 4(a).

Institution of an *inter partes* review is authorized by statute when "the information presented in the petition . . . and any response . . . 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." 35 U.S.C. § 314; *see* 37 C.F.R. §§ 42.4, 42.108. Upon considering the Petition and the Preliminary Response, we determine that Petitioner has not shown a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim. Accordingly, we decline to institute an *inter partes* review of claims 1–20 of the '680 Patent.

A. Related Applications and Proceedings

The '680 Patent shares substantially the same specification with U.S. Patent Nos. 6,774,122 B2 ("the '122 Patent"), 7,456,160 B2 ("the '160 Patent"), and 8,466,139 B2 ("the '139 Patent), which are related as follows. The '139 Patent issued from Application No. 13/602,667, which is a continuation of Application No. 12/285,877 (now the '680 Patent), which is a continuation of Application No. 10/872,784 (now the '160 Patent), which is a continuation of Application No. 09/756,291 (now the '122 Patent).

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[1] Petitioner further identifies Mylan Institutional LLC, Mylan Laboratories Limited, Agila Specialties Inc., Mylan Teoranta, Mylan Inc., and Mylan N.V. as real parties-in-interest. Pet. 2.

This chain of continuations was first filed on January 9, 2001, and each patent in the family claims benefit of foreign priority to applications filed April 12, 2000, and January 10, 2000. Petitioner acknowledges that the earliest possible priority date for the '680 Patent is January 10, 2000. *See* Pet. 10.

According to the parties, the '680 Patent has been the subject of numerous district court litigations. *See* Pet. 2–3; Paper 4, 2–3; Paper 6, 2–3; Paper 8, 2; Paper 9, 2. The parties further indicate that the '139, '160, and '122 Patents are also involved in the district court proceedings. Paper 4, 2, Paper 6, 2; Paper 8, 2; Paper 9, 2.

In addition to the instant Petition challenging claims 1–20 of the '680 Patent, Petitioner has submitted Petitions challenging claims of the '122 Patent (IPR2016-01316), the '160 Patent (IPR2016-01324), and the '139 Patent (IPR2016-01326).

B. The '680 Patent and Relevant Background

The invention relates to "a novel sustained release pharmaceutical formulation adapted for administration by injection containing the compound 7a-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol," also known in the art as ICI 182,780 or fulvestrant. Ex. 1001, Abstract; 1:65–2:2. The Specification teaches intramuscular injection of the disclosed fulvestrant formulation for the treatment of "benign or malignant diseases of the breast or reproductive tract, preferably treating breast cancer." *Id.* at 11:14–16.

As of the filing date of the '680 Patent, nonsteroidal antiestrogens, most particularly, tamoxifen, were used in the treatment of hormonal-dependent breast cancers. *See* Pet. 8–9; Prelim. Resp. 18–19; Ex. 1001,

1:23–36. In some hormonal-dependent cancers, estrogen bound to estrogen receptors (ERs) stimulates tumor growth. *See* Pet. 9; Prelim. Resp. 20. Tamoxifen is a selective estrogen receptor modulator or SERM, meaning that it acts as an estrogen antagonist in hormonal-dependent breast cancers, blocking the binding of estrogen to its receptors; conversely it also acts like an estrogen agonist in other tissues, providing beneficial effects in bone and heart, and potentially detrimental effects in uterine tissue. *See* Pet. 9; Prelim Resp. 20–21. In addition, resistance to tamoxifen tends to develop over time, resulting in resumed tumor growth. *See* Pet. 19; Prelim. Resp. 20; Ex. 1001, 2:13–19. Accordingly, researchers sought alternative treatments for estrogen-dependent breast cancers. *See* Prelim. Resp. 21–23. Of these, fulvestrant was under investigation as of the filing date of the '680 Patent. *See* Prelim. Resp. 23–24; Ex. 1001, 2:5–20, 58–64. Unlike tamoxifen, fulvestrant is a steroidal antiestrogen, and does not display the ER agonist activity of tamoxifen. *See* Pet. 9; Prelim. Resp. 22; Ex. 1001, 2:13–20, 31–39. Rather, fulvestrant is considered a "pure" antiestrogen or ERD (estrogen receptor downregulator). *See* Pet. 9; Prelim. Resp. 22.

The Specification discloses that intramuscular administration of fulvestrant in aqueous suspension results in a clinically insufficient release rate and "extensive local tissue irritation" because fulvestrant particles are present at the injection site. Ex. 1001, 8:62–9:5. And while the "solvating ability of castor oil for steroidal compounds is known" (*id.* at 5:48–53), a monthly depot injection made by dissolving fulvestrant in castor oil alone would require formulation volumes of at least 10 ml "to achieve a high enough concentration to dose a patient in a low volume injection and

achieve a therapeutically significant release rate." *Id.* at 5:54–6:2. In addressing these problems, the Patent states that,

> With the addition of high concentrations of an alcohol concentrations of >50 $mgml^{-1}$ of fulvestrant in a castor oil formulation is achievable, thereby giving an injection volumes of <5 ml. . . . We have surprisingly found that the introduction of a non-aqueous ester solvent which is miscible in the castor oil and an alcohol surprisingly eases the solubilisation of fulvestrant into a concentration of at least 50 $mgml^{-1}$. . . . The finding is surprising since the solubility of fulvestrant in non-aqueous ester solvent . . . is significantly lower than the solubility of fulvestrant in an alcohol. . . . [or] in castor oil.

Id. at 6:3–18 (referencing Tables 2 and 3).

The Specification, thus, describes the extended release fulvestrant formulation of the invention as comprising

> Fulvestrant . . . in a ricinoleate vehicle,[2] a pharmaceutically acceptable nonaqueous ester solvent, and a pharmaceutically acceptable alcohol wherein the formulation is adapted for intramuscular administration and attaining a therapeutically significant blood plasma fulvestrant concentration for at least 2 weeks.

Ex. 1001, 6:20–27. In preferred embodiments, the ricinolate vehicle is castor oil, the alcohol is a combination of ethanol and benzyl alcohol, and the non-aqueous ester solvent is benzyl benzoate. *Id.* at 7:43–57; 8:55–58.

The Specification explains that "extended release" means that "at least two weeks, at least three weeks, and, preferably at least four weeks of continuous release of fulvestrant is achieved," and that "therapeutically

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[2] The Specification defines ricinolate vehicles as castor oil and other oils having "at least 20% . . . of its composition as triglycerides of ricinoleic acid." *Id.* at 5:47–53; 8:52–27.

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