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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FRESENIUS-KABI USA LLC,
Petitioner,

v.

ASTRAZENECA AB,
Patent Owner.

Case IPR2017-01910
Patent 6,774,122 B2

Before GRACE KARAFFA OBERMANN, ZHENYU YANG, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

OBERMANN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner Fresenius-Kabi USA LLC ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1, 2, 5, and 9 U.S. Patent No. 6,774,122 B2 (Ex. 1001, "the '122 Patent"). Paper 1 ("Pet."). AstraZeneca AB ("Patent Owner") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp.").

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 the '122 Patent.

A. *Related Applications and Proceedings*

The '122 Patent shares substantially the same specification with U.S. Patent Nos. 7,456,160 B2 ("the '160 Patent"), 8,329,680 B2 ("the '680 Patent"), and 8,466,139 B2 ("the '139 Patent), which are related as follows. The '139 Patent issued from Application No. 13/602,667 ("the '667 Application"), which is a continuation of Application No. 12/285,887 ("the '887 Application") (now the '680 Patent), which is a continuation of Application No. 10/872,784 ("the '784 Application") (now the '160 Patent), which is a continuation of Application No. 09/756,291("the '291 Application") (now the '122 Patent). 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.

According to the parties, the '122 Patent has been the subject of numerous district court litigations. *See* Pet. 4–5; Paper 6, 2–3. According to Patent Owner, the

related ’160, ’680, and ’139 Patents have also been involved in district court proceedings. Paper 6, 3.

Each of the four related patents have also been the subject of *inter partes* review proceedings filed by Mylan Pharmaceuticals, Inc. (“Mylan”). Of these, IPR2016-01316 on the ’122 patent, IPR2016-01324 on the ’160 patent, and IPR2016-01326 on the ’139 patent were terminated before we issued a decision regarding institution. In IPR2016-01325 (“the Mylan IPR”) on the ’680 patent, however, we issued a Decision denying institution (“Mylan Decision”), which Petitioner submits in this proceeding as Exhibit 1011 and discusses extensively in the Petition.

The ’122 patent and two related patents also have been the subject of petitions for *inter partes* review filed by InnoPharma Licensing, LLC: IPR2017-00904 on the ’122 patent, IPR2017-00900 on the ’680 patent, and IPR2017-00905 on the ’139 patent. We previously denied each of those petitions.

In addition to the instant Petition challenging claims of the ’122 Patent, Petitioner has submitted Petitions challenging claims of the ’139 Patent (IPR2017-01912) and the ’680 Patent (IPR2017-01913). These petitions are virtually identical to the three petitions filed by InnoPharma Licensing and denied by the Board in IPR2017-00900, IPR2017-00904, and IPR2017-00905, respectively. Paper 7, 3–4; *see id.* at 4 (“Petitioner copied verbatim the earlier-filed petitions, and supporting declarations, submitted by InnoPharma Licensing.”). Petitioner filed requests for joinder with the respective *inter partes* reviews filed by InnoPharma (Paper 3), which we denied (Paper 7).

B. The ’122 Patent and Relevant Background

The Specification of the ’122 Patent discloses “an extended release pharmaceutical formulation adapted for intra-muscular injection comprising fulvestrant” [1] for the treatment of “benign or malignant disease[s]of the breast or

1 The Specification defines “extended release” to mean that “at least two weeks, at least three weeks, and, preferably at least four weeks of continuous release of fulvestrant is achieved.”

reproductive tract, preferably treating breast cancer." Ex. 1001, 10:56–11:22. Fulvestrant is also known in the art as ICI 182,780 or 7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17-β-diol, and is the active ingredient in AstraZeneca's FASLODEX product for "[t]reatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy." *Id*. at Abstract; 1:64–2:2; Ex. 1021,[2] 1, 13.

As of the filing date of the '122 Patent, nonsteroidal antiestrogens, most particularly, tamoxifen, were used in the treatment of hormone-dependent breast cancers. *See* Ex. 1001, 1:16–32; Prelim. Resp. 19–20. In some hormone-dependent cancers, estrogen bound to estrogen receptors (ERs) stimulates tumor growth. *See* Pet. 12; Prelim. Resp. 19. Tamoxifen is a selective estrogen receptor modulator or SERM, meaning that it acts as an estrogen antagonist in these cancers, blocking the binding of estrogen to its receptors. Prelim Resp. 19–20. As of the filing date of the '122 Patent, however, researchers were seeking alternative treatments, including fulvestrant, for estrogen-dependent breast cancers because resistance to tamoxifen tends to develop over time, and because tamoxifen treatment could adversely affect bone and uterine tissue. *See* Ex. 1001, 2:11–31; Prelim. Resp. 19–21; Ex. 1015 ¶¶ 61–74. Unlike tamoxifen, fulvestrant is a "pure" antiestrogen or ERD (estrogen receptor downregulator), which does not display the partial ER agonist activity of tamoxifen. *See* Ex. 1001, 2:12–19; Ex. 1015 ¶¶ 61, 77.

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, 8:36–46. And while the "solvating ability of castor oil for steroidal compounds is known" (*id*. at 5:19–24), a monthly depot injection made by dissolving

Id. at 9:17–9.

2 FASLODEX Prescribing Information, Rev. 11/2012.

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 5:25–41. In addressing these problems, the '122 Patent states:

> 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 solvents . . . is significantly lower than the solubility of fulvestrant in an alcohol. . . . [or] in castor oil.

Id. at 5:44–57 (referencing Tables 2 and 3); *see also id*. at 9:23–47 ("Table 3 shows . . . . the positive effect of benzyl benzoate on fulvestrant solubility in castor oil, despite fulvestrant having a lower solubility in benzyl benzoate than in either alcohol or castor oil.").

The Specification further discloses that "[s]imply solubilising fulvestrant in an oil based liquid formulation is not predictive of a good release profile or lack of precipitation of drug after injection at the injection site." *Id.* at 9:20–22. But according to the inventors, in vivo testing of the castor oil-based formulations of the invention "surprisingly" demonstrates, "after intra-muscular injection, satisfactory release of fulvestrant over an extended period of time." *Id.* at 8:29–32. In particular, Figure 1 shows release profiles after intramuscular injection into rabbits of 5% fulvestrant formulations comprising 10% ethanol, 10% benzyl alcohol and 15% benzyl benzoate made to volume with various oil components. *See id*. at 9:54–10:55, Fig. 1. The inventors conclude that "the castor oil formulation showed a particularly even release profile with no evidence of precipitation of fulvestrant at the injection site." *Id*. at 10:52–55; *see id*. at Fig. 1 and Table 4, second half.

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