IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

OSI PHARMACEUTICALS, INC., PFIZER, INC., and GENENTECH INC.,	)	
Plaintiffs,	)	
v.	)	Civ. No. 09-185-SLR
MYLAN PHARMACEUTICALS INC.,	)	
Defendant.	)	

Jack B. Blumenfeld, Esquire and Maryellen Noreika, Esquire of Morris, Nichols, Arsht & Tunnell LLP. Counsel for Plaintiffs. Of Counsel: Leora Ben-Ami, Esquire, Benjamin Hsing, Esquire, Daniel Bogliogi, Esquire and Sapna W. Palla, Esquire of Kaye Scholer LLP.

John C. Phillips, Jr., Esquire and Megan Haney, Esquire of Phillips, Goldman & Spence, P.A. Counsel for Defendant. Of Counsel: James H. Wallace, Jr., Esquire, Mark A. Pacella, Esquire, Matthew J. Dowd, Esquire and Adrienne Johnson, Esquire of Wiley Rein LLP.

OPINION

Dated: May 1, 2012
Wilmington, Delaware

ROBINSON, District Judge

I. INTRODUCTION

This action arises out of the filing of Abbreviated New Drug Applications ("ANDAs") by Mylan Pharmaceuticals Inc. ("Mylan") and Teva Pharmaceuticals USA, Inc. ("Teva") seeking to market generic versions of Tarceva® (erlotinib tablets), used to treat certain indications of non-small cell lung cancer and pancreatic cancer. Plaintiff OSI Pharmaceuticals, Inc. ("OSI") is the holder of approved New Drug Application ("NDA") No. 021743 for Tarceva®. OSI and plaintiff Pfizer, Inc. ("Pfizer") are owners of U.S. Patent Nos. 5,747,498 ("the '498 patent"), 6,900,221 ("the '221 patent") and 7,087,613 ("the '613 patent"). Plaintiff Genentech Inc. ("Genentech") is a "co-exclusive licensee" of these patents, which are listed in the Food and Drug Administration's ("FDA's") publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" (known as the "Orange Book")[1] for Tarceva®. (D.I. 54 at ¶¶ 14, 19, 21) In December 2009, the '498 patent was reissued as U.S. Reissue Patent No. RE 41,065 ("the RE '065 patent"), which has been added to the Orange Book for Tarceva®.

In February 2009, OSI and Pfizer received a letter from Teva notifying them that Teva had filed ANDA No. 91-059 with a Paragraph IV certification[2] alleging that the '498, '221 and '613 patents are invalid, unenforceable, and/or not infringed by Teva's generic erlotinib hydrochloride tablets. (*Id.* at ¶ 26) Shortly thereafter, also in February 2009, Mylan sent notice to OSI and Genentech that Mylan filed ANDA No. 91-002 with a

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[1]The Orange Book must list "each drug which has been approved for safety and effectiveness through an NDA." *See* 21 U.S.C. §§ 355(j)(A)(ii).

[2]*See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

Paragraph IV certification alleging that the '498, '221 and '613 patents are invalid, unenforceable, and/or not infringed by Mylan's generic erlotinib hydrochloride tablets. (*Id.* at ¶ 31) On March 19, 2009, plaintiffs filed Civ. Nos. 09-185 and 09-186, alleging infringement of the '498, '221 and '613 patents by Teva and Mylan, respectively.[3] The cases were consolidated. In January 2010, after the issuance of the RE '065 patent, plaintiffs filed an amended and supplemental consolidated complaint in Civ. No. 09-185, alleging infringement of the RE '065, 221 and '613 patents by Teva and Mylan. (*Id.*) Teva and Mylan brought counterclaims for noninfringement and for invalidity. (D.I. 56, 57)

After the close of fact discovery, Teva moved to amend its pleadings to add the defenses of invalidity based on obviousness-type double-patenting; the court denied the motion. (D.I. 172, 213) A pretrial conference was held March 3, 2011. Teva and Mylan conceded infringement of claims 1, 2, 4, 8, 34 and 35 of the RE '065 patent and claim 53 of the '221 patent. (D.I. 198 at 2) On March 11, 2011, the court denied Teva's motion for reconsideration of the court's denial of its motion to amend. (D.I. 218) A settlement was reached between plaintiffs and Teva on the eve of trial. (D.I. 222, 223) Mylan presented its invalidity defenses during a five-day bench trial commencing March 14, 2011. On June 30, 2011, the court entered an order enjoining Mylan from launching its generic product until the court's decision issued. (D.I. 231) The validity issues have been fully briefed post-trial. (D.I. 232, 233, 234) The parties represent that the 30-

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[3] *See* 35 U.S.C. § 271(e)(2)(A) ("(2) It shall be an act of infringement to submit – (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent[.]").

month statutory stay expires "on or about May 18, 2012."[4] (D.I. 232 at 1; D.I. 233 at 3)

The court has jurisdiction pursuant to 28 U.S.C. §§ 1331, 1338(a) and 1400(b). Having considered the documentary evidence and testimony, the court makes the following findings of fact and conclusions of law pursuant to Fed. R. Civ. P. 52(a).

II. FINDINGS OF FACT AND CONCLUSIONS OF LAW

A. The Technology at Issue

1. EGFR and NSCLC

1. A discussion of the technology at issue is best framed by an overview of epidermal growth factor receptor ("EGFR") and its role vis-a-vis cancer cells. EGFR is a receptor tyrosine kinase that is involved in transmitting signals from the outside of a cell to the inside of a cell. In normal cells, epidermal growth factor (or "EGF") binds to EGFR, which will cause a second EGFR or one of its family members together to bind to it, resulting in the transfer of a phosphate to the EGFR. This phosphorylation "initiates a cascade of signalling events within the cell, leading to increased survival and increased cell proliferation[.]" (D.I. 226 at 466:14-467:2) A EGFR tyrosine kinase inhibitor is a small molecule that penetrates a cell, binds to the catalytic portion of the kinase, and inhibits its enzymatic activity in transferring a phosphate. (*Id.* at 467:5-8) There are also EGFR kinase inhibitors that are not tyrosine kinase inhibitors, such as monoclonal antibodies that bind to EGFR, that are not the subject of the patents in suit. (*Id.* at 467:18-23)

2. Receptor tyrosine kineases are "frequently aberrantly expressed in common

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[4] *See* 21 U.S.C. § 355(j)(5)(B)(iii).

human cancers," and "[i]t has also been shown that epidermal growth factor receptor (EGFR) which possesses tyrosine kinase activity is mutated and/or overexpressed in many human cancers[.]" (RE '065, col. 1:24-48)

3. There are two general types of lung cancer: non-small cell lung cancer ("NSCLC"), making up 80-85% of cases, and small-cell lung cancer ("SCLC"), which is about 10-15% of all lung cancers. (D.I. 227 at 806:18-24 (85%/15% ratio); DTX-365 at 365 (80% of lung cancers classified as NSCLC, and 10% have both small-cell and non-small cell elements)) NSCLC is further divided into three types: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. (D.I. 224 at 70:17-24) Doctors' classification of the cancer is important because NSCLC and SCLC have "distinct morphology, genetics, biology and clinical behavior." (DTX-433 at 310)

2. Erlotinib

4. Erlotinib, or N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine (formula $C_{22}H_{23}N_3O_4$), is a kinase inhibitor.[5] The structure of erlotinib is below, highlighted to differentiate the molecule's functional segments: the quinalone core (yellow); an anilino group comprised of the amine linker (purple); an analine ring (orange); 3'-position substitution with an ethynyl substituent (red); and substitution at the 6,7-potisions with dimethoxyethoxy tails (green).

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[5] *See gen.* PubChem, *erlotinib - Compound summary*, available at http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=176870&loc=ec_rcs.

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