

2012-1431

**UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT**

---

OSI PHARMACEUTICALS, INC., PFIZER INC.,  
and GENENTECH, INC.,

*Plaintiffs-Appellees,*

v.

MYLAN PHARMACEUTICALS INC.,

*Defendant-Appellant.*

Appeal from the United States District Court for the District of Delaware  
in case no. 09-CV-0185, Judge Sue L. Robinson.

---

**BRIEF OF PLAINTIFFS-APPELLEES OSI PHARMACEUTICALS, INC.,  
PFIZER INC., AND GENENTECH, INC.**

---

Benjamin C. Hsing  
Sapna W. Palla  
KAYE SCHOLER LLP  
425 Park Avenue  
New York, NY 10022  
Tel: (212) 836-8000

Leora Ben-Ami  
KIRKLAND & ELLIS LLP  
601 Lexington Avenue  
New York, NY 10022  
Tel: (212) 446-5943

*Attorneys for Plaintiffs-Appellees OSI  
Pharmaceuticals, Inc., Pfizer Inc.,  
and Genentech, Inc.*

## CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47.4, counsel for the Plaintiffs-Appellees, OSI Pharmaceuticals, Inc., Pfizer Inc., and Genentech, Inc. certifies the following:

1. The full name of every party or amicus represented by me is:

OSI Pharmaceuticals, Inc, Pfizer Inc. and Genentech, Inc.

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

OSI Pharmaceuticals, LLC (formerly known as OSI Pharmaceuticals, Inc.)<sup>1</sup>.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

OSI Pharmaceuticals, LLC is a wholly owned subsidiary of Astellas US LLC, which is a wholly owned subsidiary of Astellas US Holding, Inc. Astellas US Holding, Inc. is a wholly owned subsidiary of Astellas Pharma Inc., a Japanese company. Astellas Pharma Inc. is publicly traded on the Tokyo and Osaka stock exchanges and no publicly held corporation owns more than 10% of the stock of Astellas Pharma Inc.

Pfizer Inc. has no parent corporations and no publicly held corporation owns 10% or more of its stock.

Genentech, Inc. is a wholly owned subsidiary of Roche Holdings, Inc. Roche Holding, Inc.'s ultimate parent, Roche Holding Ltd., is publicly traded on the Swiss Stock Exchange. Upon information and belief, more than 10% of Roche Holding Ltd.'s voting shares are held either directly or indirectly by Novartis AG, a publicly held Swiss corporation.

---

<sup>1</sup> As of March 31, 2011, OSI Pharmaceuticals, Inc. became OSI Pharmaceuticals, LLC in accordance with Section 18-214 of the Delaware Limited Liability Company Act.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

Benjamin C. Hsing  
Sapna W. Palla  
Kaye Scholer LLP  
425 Park Avenue  
New York, NY 10022  
Tel: (212) 836-8000  
Fax: (212) 836-8689

Jack B. Blumenfeld  
Maryellen Noreika  
Morris, Nichols, Arsht & Tunnell, LLP  
1201 North Market Street  
P.O. Box 1347  
Wilmington, DE 19899-1347  
Tel: (302) 658-9200  
Fax: (302) 658-3989

Leora Ben-Ami  
Kirkland & Ellis LLP  
601 Lexington Avenue  
New York, NY 10022  
Tel: (212) 446-5943  
Fax: (212) 446-6460

Date: September 27, 2012

/s/ Benjamin C. Hsing  
Signature of counsel

Benjamin C. Hsing  
Printed name of counsel

## TABLE OF CONTENTS

	<u>Page</u>
STATEMENT OF RELATED CASE .....	1
STATEMENT OF THE ISSUES.....	2
STATEMENT OF THE CASE.....	4
STATEMENT OF FACTS .....	6
I. PATENTS-IN-SUIT .....	6
A. The RE'065 Patent .....	6
B. The '221 Patent .....	6
II. ERLOTINIB .....	7
III. THE PRIOR ART TO THE RE'065 PATENT.....	7
A. Zeneca's '722 Application .....	7
B. Zeneca's '226 Application .....	8
C. The Barker Abstracts.....	8
D. The Fry Science Article.....	9
IV. FAILED EGFR TYROSINE KINASE INHIBITORS .....	10
V. THE DISCOVERY OF ERLOTINIB .....	11
A. Pfizer's Discovery Of The 4-Anilinoquinazoline Core .....	12
B. Pfizer's Strategy To Modify The 4-Anilinoquinazoline Core .....	12
C. Pfizer's Discovery Of A Compound Substituted With 6,7-Dimethoxyethoxy Tails .....	15
D. Pfizer's Discovery Of A Compound Substituted With An Ethynyl Group .....	15
E. Pfizer's Discovery of Erlotinib .....	17
VI. PFIZER'S DISCOVERY OF ERLOTINIB FOR THE TREATMENT OF NSCLC .....	18

VII. THE ROLE OF EGFR OVEREXPRESSION WAS UNCLEAR IN 1999 .....	20
VIII. THE REFERENCES CITED BY MYLAN AGAINST CLAIM 53.....	22
A. The '498 Patent .....	22
B. The Cold Spring Harbor Abstract .....	23
C. AACR Abstracts.....	23
D. The Moyer Article .....	23
E. The Klohs Article .....	24
F. OSI Press Release And 10-K .....	24
G. ASCO Abstracts .....	25
IX. FDA APPROVAL OF ERLOTINIB FOR NSCLC AND PANCREATIC CANCER.....	26
SUMMARY OF ARGUMENT .....	27
ARGUMENT .....	30
I. The District Court Correctly Held That The RE'065 Patent Was Not Obvious.....	30
A. The Law Of Obviousness.....	30
B. Mylan's Obviousness Argument Is Legally Incorrect .....	33
C. A Person of Ordinary Skill In The Art Would Not Have Selected Example 51 As A Lead Compound.....	33
D. Persons Of Ordinary Skill Would Not Have Modified The Example 51 Compound To Arrive at Erlotinib.....	40
1. Persons of Ordinary Skill Would Have Modified The Anilinoquinazoline Core.....	40
2. The Prior Art Taught A Preference For Halogens.....	41
3. A Person Of Skill Would Not Have Selected An Ethynyl Group As A Substituent .....	42
4. The Barker Abstracts Did Not Teach An Ethynyl Group.....	43
5. The Prior Art Taught Away From Using An Ethynyl Group.....	46

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.