

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.
Petitioner,

v.

ASTRAZENECA AB
Patent Owner.

U.S. Patent No. 8,466,139

**DECLARATION OF LESLIE OLEKSOWICZ, M.D.
IN SUPPORT OF PETITION FOR *INTER PARTES* REVIEW OF
U.S. PATENT NO. 8,466,139**

TABLE OF CONTENTS

I.	QUALIFICATIONS AND BACKGROUND	5
A.	Education and Experience.....	5
B.	Materials Considered	9
C.	Scope of Work	9
II.	SUMMARY OF OPINIONS	10
III.	LEGAL STANDARDS	11
IV.	PERSON OF ORDINARY SKILL IN THE ART.....	13
V.	U.S. PATENT NO. 8,456,139 (“THE ’139 PATENT”) [Ex. 1001].....	14
VI.	CLAIM CONSTRUCTION.....	17
VII.	BACKGROUND OF BREAST CANCER AND TREATMENTS.....	18
A.	Hormone Receptor Positive (HR+) Breast Cancer in Human Females.....	18
B.	Treatment Options for HR+ Breast Cancer in Women Prior to 2000.....	19
VIII.	SCOPE AND CONTENT OF THE PRIOR ART REFERENCES	22
A.	McLeskey 1998 [Ex. 1005].....	22
B.	Howell 1996 [Ex. 1006].....	23
C.	Dukes 1989 [Ex. 1007]	26
D.	Wakeling 1991 [Ex. 1008].....	26
E.	Wakeling 1992 [Ex. 1009].....	28
F.	Dukes 1992 [Ex. 1025]	29
G.	Wakeling 1993 [Ex. 1028].....	30
H.	Dukes 1993 [Ex. 1026]	32
I.	DeFriend 1994 [Ex. 1027]	34
J.	Osborne 1995 [Ex. 1018].....	36
K.	Howell 1995 [Ex. 1012].....	37
L.	O’Regan 1998 [Ex. 1013].....	38
IX.	FULVESTRANT WAS A WELL UNDERSTOOD COMPOUND BY JANUARY 10, 2000.....	40
A.	Fulvestrant Was Well Known in the Prior Art.....	40
B.	Fulvestrant’s Pharmacological Usefulness Was Well Known in the Prior Art.	40
C.	Fulvestrant’s Pre-Clinical Anti-Tumor and Anti-Uterotrophic Effects Were Well Known in the Prior Art.	41

D.	Fulvestrant’s Clinical Efficacy in Human Females With Breast Cancer Was Well Known in the Prior Art.....	46
E.	Fulvestrant’s Efficacy in Human Females with ER+ Breast Cancer was Well Known in the Prior Art.....	48
F.	Fulvestrant Formulations and Its Intramuscular Route of Administration Were Established in the Prior Art.	49
1.	Indication	49
2.	Excipients and Percent w/v Concentrations.....	50
3.	Route and Schedule of Administration.....	52
4.	Dose of Fulvestrant As-Formulated.....	54
5.	Divided Dose	55
6.	Fulvestrant Concentration of About 50 mgml ⁻¹	56
7.	Fulvestrant Total Dose of 250 mg	56
X.	UNPATENTABILITY OF THE ’139 PATENT.....	57
A.	Claims 1–20 of the ’139 patent were obvious over McLeskey.	58
1.	McLeskey disclosed the claimed fulvestrant formulation.	58
2.	The prior art disclosed the use of fulvestrant to treat human females having HR+ breast cancer.	59
3.	The prior art disclosed delivering fulvestrant intramuscularly to humans.	60
4.	The prior art disclosed administering a formulation having a concentration of about 50 mg/ml of fulvestrant to human females having breast cancer.....	61
5.	A POSA knew from the prior art to administer to humans a 5 ml volume of formulated fulvestrant.....	62
6.	A POSA would have understood that the 5 ml of formulated fulvestrant could have been administered to a human female in a divided dose.	63
7.	A POSA would have understood that the fulvestrant formulation could have been administered monthly.....	64
8.	A POSA would have understood that the claimed blood plasma fulvestrant concentrations were not limitations of the patent.	65
B.	All claims of the ’139 patent were obvious over Howell 1996 in view of McLeskey.....	67
1.	Howell 1996 disclosed using fulvestrant to treat breast cancer in a human female.....	68

2.	Howell 1996 in view of McLeskey disclosed administering McLeskey's complete fulvestrant formulation to a human, particularly a human female.....	69
3.	Howell 1996 in view of McLeskey disclosed administering 5 ml of fulvestrant intramuscularly to a human female with breast cancer.....	70
4.	A POSA would have known to administer the 5 ml of formulated fulvestrant in a divided dose.	72
5.	A POSA would have known to administer the fulvestrant formulation to a human monthly.....	73
6.	Howell 1996 in view of McLeskey disclosed administering a fulvestrant formulation of 50 mg/ml concentration to a human female with breast cancer.....	74
7.	A POSA would have understood that the claimed blood plasma fulvestrant concentrations were not limitations of the patent.	75
8.	Even to the extent the claimed blood plasma fulvestrant concentrations are limitations, they were disclosed by Howell 1996, alone or in view of McLeskey.	76
XI.	CONCLUSION.....	78

I. QUALIFICATIONS AND BACKGROUND

A. Education and Experience

1. My name is Leslie Oleksowicz. I am a physician and oncologist with over thirty years of experience, spending over 25 years in clinical practice. Throughout my career I have conducted clinical research in the field of Medical Oncology, participated in over 100 clinical trials, and written over 75 publications in my area of expertise. I have treated hundreds of patients with all stages and subtypes of breast cancer, and I directed a basic science laboratory research effort from 1992–2000 which focused on breast cancer adhesive receptors and their role in tumor metastases. In my role as CEO of Leslie Oleksowicz, M.D., LLC, I have also acted as a consultant to provide strategic intelligence to the financial and pharmaceutical industries, advising expertise to biotech and EMR (electronic health medical record) start-up companies and expert skills in legal cases involving intellectual property in the context of oncologic pharmaceuticals. My full *curriculum vitae* (CV) is attached hereto as Exhibit A and is incorporated herein.

2. I received my B.A. in Biological Sciences from Amherst College in 1978, graduating *magna cum laude* and Phi Beta Kappa. I received my M.D. from Tufts University School of Medicine in 1982.

3. After finishing medical school, I completed postgraduate training Internship and Residency Programs in Internal Medicine in 1985 at the Albert

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.