

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE PATENT TRIAL AND APPEAL BOARD

---

APOTEX INC., APOTEX CORP., ARGENTUM PHARMACEUTICALS LLC,  
ACTAVIS ELIZABETH LLC, TEVA PHARMACEUTICALS USA, INC., SUN  
PHARMACEUTICAL INDUSTRIES, LTD., SUN PHARMACEUTICAL  
INDUSTRIES, INC., AND SUN PHARMA GLOBAL FZE,

Petitioners,

V.

NOVARTIS AG,

Patent Owner.

---

Case IPR2017-00854<sup>1</sup>

U.S. Patent No. 9,187,405

---

**SECOND DECLARATION OF WILLIAM J. JUSKO, PH.D.**

Mail Stop Patent Board  
Patent Trial and Appeal Board  
U.S. Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450

---

<sup>1</sup> Cases IPR2017-01550, IPR2017-01946, and IPR2017-01929 have been joined with this proceeding.

**Anotex v. Novartis**

## TABLE OF CONTENTS

	<b>Page</b>
I. Introduction.....	1
II. A Person of Ordinary Skill in the Art.....	9
III. The Subjects of Pharmacokinetics and Pharmacodynamics .....	12
IV. The Many “Perplexities” of Fingolimod .....	18
V. Pharmacologist’s View of the State of the Art.....	21
A. No Difference Between 5.0 and 1.25 mg in Human Multiple Sclerosis Phase II Results – Kappos 2005 .....	22
B. Art Taught 80% Lymphocyte Suppression Needed To See Efficacy in Human Transplant Clinical Studies .....	24
C. Art Taught 70% Lymphocyte Suppression Needed To See Efficacy in EAE Model of RRMS .....	32
D. Pharmacokinetic and Pharmacodynamic Modeling.....	42
VI. The ’405 Patent.....	46
VII. The Novartis Report .....	49
VIII. Dr. Giesser Uses Terms Differently Than a Person Of Ordinary Skill.....	54
A. Lymphopenia Is Not a “Clinical End-Point” for MS.....	54
B. A Pharmacologic Effect May or May Not Be Therapeutic .....	58

C	“Daily” Dose Does Not Mean a One-Time Administration .....	59
D.	FTY, FTY720, Fingolimod and the HCl Salt Used Interchangeably.....	60
IX.	Dr. Giesser’s Disagreement with Novartis’ Statements in the ’405 Patent File History Are Based on Misreading Kovarik and an Incorrect Equation in an Off-Point Textbook .....	63
A.	Dr. Giesser Misreads Kovarik.....	63
B.	Dr. Giesser Relies on a Mistake In an Off-Topic Textbook .....	64
X.	Claims Were Not Obvious to A Person of Ordinary Skill in the Art.....	67
XI.	Ground 1 – Kovarik and Thomson .....	69
A.	Kovarik Would Not Be Considered Relevant to a Person of Skill.....	70
B.	The Board Misunderstood the Loading Dose Notation in Kovarik .....	71
C.	Dr. Giesser Misconstrues the Word “Daily”.....	73
D	“Standard Daily Dose” in Kovarik Presumes Effectiveness Was Already Established .....	74
E.	No Motivation to Combine Kovarik with Thomson.....	77
F.	Thomson Does Not Fix the Deficiencies of Kovarik.....	78
XII.	Ground 2 – Chiba and Budde and Kappos 2005 .....	80
XIII.	Ground 3 – Kappos 2010.....	86

XIV. Conclusion .....89

I, William J. Jusko, Ph.D., declare as follows:

## **I. Introduction**

1. I previously submitted a May 2, 2017 declaration in this IPR, Exhibit 2005. I am a Professor of Pharmaceutical Sciences with over 50 years of experience and over 600 research articles in the area of pharmaceutical sciences. I have extensive experience in the design of pre-clinical and human clinical trials. My work has focused on the pharmacology of immunosuppressants and changes in cell trafficking that result. I have studied and published on the pharmacokinetics and pharmacodynamics of fingolimod in several animal species. My full qualifications and expertise are set out in my first declaration along with my *curriculum vitae* and publication list.

2. I understand that Apotex and now other companies have filed Petitions challenging the validity of U.S. Patent No. 9,187,405 (“’405 Patent”), owned by Novartis. The ’405 Patent claims methods for ameliorating relapsing-remitting multiple sclerosis (RRMS) by administering 0.5 mg daily of fingolimod without a preceding loading dose. Since the submission of my first declaration, I understand the Board has instituted this IPR.

3. Counsel for Patent Owner Novartis asked me to review the Petitions in view of the Board’s Institution Decision, focusing on the declaration from Dr. Barbara Giesser, Exhibit 1002. I understand Novartis filed an application for the

# 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.