

UNITED STATES PATENT AND TRADEMARK OFFICE

---

**BEFORE THE PATENT TRIAL AND APPEAL BOARD**

---

APOTEX INC. and APOTEX CORP.,

Petitioners,

v.

NOVARTIS AG,

Patent Owner.

---

Case IPR2017-00854

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

---

**PRELIMINARY PATENT OWNER RESPONSE**

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

## TABLE OF CONTENTS

<b>PRELIMINARY STATEMENT</b> .....	1
<b>FACTS</b> .....	5
A. The State of the Art in Fingolimod Research in June 2006 .....	6
1. Fingolimod’s Discovery and Early Research on its Mechanism of Action .....	6
2. Fingolimod and Transplant Research.....	7
3. Fingolimod and MS Research .....	9
B. The Inventors’ Neo-Angiogenesis Discovery and the ’405 Patent.....	13
1. The Invention .....	13
2. Prosecution .....	15
3. The Issued Claims .....	17
C. Apotex’s Petition.....	17
1. Kovarik plus Thompson.....	17
2. Chiba plus Budde plus Kappos 2005 .....	19
3. Kappos 2010.....	20
<b>ARGUMENT</b> .....	21
<b>I. Apotex’s Kovarik-Thomson Ground Fails to        Provide Any Reason to Question the Examiner’s        Decision to Allow the Patent over Kovarik</b> .....	21
A. <b>The Board Should Not Rehash Prosecution</b> .....	21
B. <b>The Examiner’s Conclusion Was Correct: Kovarik’s            Loading-Dose Requirement Teaches Away from            the ’405 Patent</b> .....	23

<b>C. Kovarik Further Never Teaches How a 0.5 mg Fingolimod Daily Dose Would Be Effective for the Claimed Methods</b> .....	29
1. <u>Apotex’s Incorrect Claim Construction</u> .....	29
2. <u>The Kovarik-Thomson Ground Fails Without Apotex’s Fatally Flawed Claim Construction</u> .....	35
<b>II. Apotex’s Chiba-Budde-Kappos 2005 Ground Fails For Lack of Expert Support</b> .....	36
<b>III. Apotex’s Kappos 2010 Ground Fails as a Disguised 112 Attack Improper in an IPR, which is Wrong in Any Event</b> .....	45
<b>CONCLUSION</b> .....	49
<b>APPENDIX A: CASES ADDRESSING A PERSON OF SKILL IN DOSING PATENT DISPUTES</b> .....	50

## PRELIMINARY STATEMENT

The Apotex Petitioners base their challenges on publications selectively recycled from the patent file history plus an opinion from a putative expert who lacks essential expertise. Nothing here supports institution.

Apotex, a generic drug maker, challenges U.S. Patent No. 9,187,405. The '405 Patent claims methods for using the immunosuppressant drug fingolimod to treat relapsing-remitting multiple sclerosis (RRMS). Novartis AG owns the Patent, and fingolimod is the active ingredient in Novartis's Gilenya<sup>®</sup>, the first solid oral treatment ever approved for RRMS. Gilenya has brought relief to tens of thousands of MS patients in the United States. The U.S. Food and Drug Administration approved Gilenya in 2010 for use with the methods in the '405 Patent.

Before the inventors discovered those methods, scientists had investigated fingolimod primarily for its potential in suppressing organ transplant rejection, not as a multiple sclerosis medicine. A decade of research in transplantation had shown that fingolimod suppressed the immune response by sequestering lymphocytes in lymphatic tissue away from the blood stream. Daily 5.0 mg doses sequestered enough lymphocytes in humans to treat organ rejection.

Novartis scientists Peter Hiestand and Christian Schnell uncovered a completely different effect of fingolimod and applied it for use in multiple sclerosis, a debilitating disease in which the immune system attacks the body's own central

nervous system. Hiestand and Schnell discovered that fingolimod inhibits the growth of blood vessels into the lesions that RRMS creates in the nervous system, thereby reducing relapses and slowing progression of the disease. No one before had ever shown that fingolimod had any therapeutic mechanism other than lymphocyte sequestration. Their discovery made possible far lower doses than previously thought could be effective.

Novartis put these discoveries into a June 2006 patent application claiming use of fingolimod to treat RRMS with a 0.5 mg daily dose. The USPTO awarded the '405 Patent in 2015. The Patent reports the discovery that fingolimod suppresses “neo-angiogenesis”—new blood vessel growth—in animal models. Based on that surprising discovery, the Patent claims 0.5 mg daily dosing for subjects in need of reducing, preventing, and/or alleviating RRMS relapses; treating the disease more broadly; and slowing its progression. The claims further exclude “a preceding loading dose regimen,” a step used in other contexts to more rapidly achieve a steady-state of a drug in the body, but unnecessary for this invention.

Apotex attacks the '405 Patent as obvious and anticipated, on three grounds.

*First*, Apotex argues that a publication the Examiner used to reject the claims in prosecution, “Kovarik” (Ex. 1004), plus another publication from the Patent’s face, “Thomson” (Ex. 1005), renders the Patent’s claims obvious.

# 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.