

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

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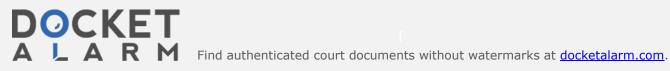


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PRELIMINARY STATEMENT

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[®], 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.



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