

STRADER, CHERILYN R., M.S. Fingolimod (Gilenya; FTY720): A Recently Approved Multiple Sclerosis Drug Based on a Fungal Secondary Metabolite and the Creation of a Natural Products Pure Compound Database and Organized Storage System. (2012) Directed by Dr. Nicholas H. Oberlies, 78 pp.

Fingolimod (Gilenya; FTY720), a synthetic compound based on the fungal secondary metabolite, myriocin (ISP-I), is a potent immunosuppressant that was approved in September 2010 by the U.S. FDA as a new treatment for multiple sclerosis (MS). Fingolimod was synthesized by the research group of Tetsuro Fujita at Kyoto University in 1992 while investigating structure-activity relationships of derivatives of the fungal metabolite, ISP-I, isolated from *Isaria sinclairii*. Fingolimod becomes active *in vivo* following phosphorylation by sphingosine kinase 2 to form fingolimod-phosphate, which binds to specific G protein-coupled receptors (GPCRs) and prevents the release of lymphocytes from lymphoid tissue. Fingolimod is orally active, which is unique among current first-line MS therapies, and it has the potential to be used in the treatment of organ transplants and cancer. The first chapter reviews the discovery and development of fingolimod, from an isolated lead natural product, through synthetic analogues, to an approved drug.

Natural products play an important role in the pharmaceutical industry, accounting for approximately half of all drugs approved in the U.S. between 1981 and 2006. Given the importance of natural product research and the vast amount of data that is generated in the process, it is imperative that the pure compounds and data are stored in a manner that will allow researchers to derive as much value as possible. The field chemoinformatics, interchangeable termed cheminformatics, has set the standards for electronic storage of chemical data, as chemistry was one of the first scientific disciplines to pursue electronic means of data storage. In this

project an electronic database was created to capture all of the relevant data for each pure compound isolated via natural product research in Dr. Oberlies lab. A system was also implemented to catalogue and store the compounds in an organized manner.

FINGOLIMOD (GILENYA; FTY720): A RECENTLY APPROVED MULTIPLE  
SCLEROSIS DRUG BASED ON A FUNGAL SECONDARY METABOLITE  
AND THE CREATION OF A NATURAL PRODUCTS PURE  
COMPOUND DATABASE AND ORGANIZED  
STORAGE SYSTEM

by

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Approved by

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APPROVAL PAGE

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