

## Drug Report - fingolimod

### Drug Summary

**Generic Name** fingolimod

**Brand Name**

**Code Name** FTY-720

**Synonym/Other**

**Mechanism of Action** sphingosine-1-phosphate receptor 1 (S1P-1) modulator; immunomodulator

**Therapy Area** acute graft rejection; graft failure; kidney graft rejection; multiple sclerosis

**Drug Class** Immunomodulators; Neuroprotectives

**Product Type** Drug

**Drug Device**

**New Mol. Entity** yes

**Originator** Mitsubishi Tanabe Pharma

**General Comments** Fingolimod inhibits T-cell trafficking by binding to sphingosine-1-phosphate receptors (the receptors on lymphocytes that respond to a molecule that signals lymphocytes to attack inflammation sites).

**Licensing Overview** Welfide (now Mitsubishi) out-licensed FTY-720 to Novartis (co SEC 20-F, 1/2007).

### Development Status

#### Indication

Treatment of primary progressive multiple sclerosis (PPMS)

#### Status Comment

Phase III INFORMS trial started Jul 2008 in Canada in patients with the primary progressive form of MS for which there are no available treatments. Primary endpoint: effect of FTY-720 relative to placebo on delaying the time to sustained disability progression; secondary endpoints: safety and tolerability of FTY-720 compared to placebo, effect of FTY-720 relative to placebo on conventional MRI parameters, effect of FTY-720 relative to placebo on patient reported outcomes (clintrial.gov, as of 10/2008).

#### Status

Phase	Region	Developer(s)	Marketer(s)
Phase III	Canada	Novartis	Novartis

#### Preparation and Method of Delivery

Oral (All)

**Indication**

Treatment of relapsing remitting multiple sclerosis (RRMS)

**Status Comment**

Data from FREEDOMS and FREEDOMS II expected in 1H:2009. Phase III (TRANSFORMS) trial met its primary endpoint; drug at 0.5 mg and 1.25 mg reduced annualized relapses with rates of 0.16 and 0.20 respectively as compared to 0.33 for interferon beta-1a and was well tolerated. Further analysis is ongoing and results will be presented in 1H:2009 (co pr, 12/2008). NDA and MAA submissions are expected Q4:2009 (co pr, 4/2008). First results from TRANSFORMS trial are to be published 1H:2009 (co slides, 9/2008). Data safety monitoring board gave approval to continue the Phase III trial, citing confounding factors in two patients who developed infections, one of which was fatal. Company anticipates filing an NDA in 2009 (Pink Sheet Daily, 6/2008). New data from Phase II study extension shows that 68-73% of patients remained relapse-free and 89% of patients were free from active brain lesions after three years of treatment; results were presented at the 60th annual meeting of the American Academy of Neurology (AAN) in Chicago (co pr, 4/2008). Phase III studies ongoing: FREEDOMS (FTY720 Research Evaluating Effects of Daily Oral therapy in Multiple Sclerosis) and FREEDOMS II trials initiated Jan 2006 and Jun 2006 respectively in the US to compare the drug with placebo during 24-months treatment period, completion expected Jul 2009 and Sep 2010 respectively (primary endpoint: relapse rate; secondary endpoints: disability progression, safety and tolerability, relapses rate in patients treated for 12 months, effect on burden of disease); multinational 12-month TRANSFORMS (TRial Assessing injectable interferon vS FTY720 Oral in RrMS) trial comparing FTY-720 to interferon beta-1a injected once-weekly initiated May 2006 in the US, Europe, Canada, Korea, Australia, completion expected Sep 2008 (primary endpoints relapse rate; secondary endpoints: proportion of relapse-free patients, safety and tolerability, burden of disease and inflammatory activity). Phase II trial initiated Sep 2007 in Japan to compare the drug with placebo during six-months treatment period, completion expected Oct 2009; primary endpoint: effect on monthly magnetic resonance imaging (MRI) lesion parameters; secondary endpoints: proportion of patients free of relapse, safety and tolerability of two doses of FTY-7-20 (clintrial.gov, as of 1/2008). Data from six-months Phase II study showed reduction of inflammatory disease activity as seen on MRI by up to 80%, and relapse rate by more than 50%. An extension of Phase II study with placebo patients switched to FTY-720 demonstrated a sustained reduction in relapses and inflammation with low disease activity maintained over two years (co SEC 20-F, 1/2007). Preclinical data suggested that in addition to its anti-inflammatory effects, FTY-720 may have the potential to reduce neurodegeneration and enhance repair of central nervous system affected by MS (co pr, 9/2006). Phase III in Europe and in the US (PAM, 6/2006). Phase II completed; Phase III planned for 4Q:2005. Phase III had previously been planned for mid-year, but is being slightly delayed due to FDA's request for an analysis of the FTY-720 safety database in transplantation, the other indication for the agent (co web, as of 6/2005).

**Status**

Phase	Region	Developer(s)	Marketer(s)
Phase III	USA	Novartis	Novartis
Phase III	Canada	Novartis	Novartis
Phase III	Australia	Novartis	Novartis
Phase III	France	Novartis	Novartis
Phase III	Germany	Novartis	Novartis
Phase III	Italy	Novartis	Novartis
Phase III	Netherlands	Novartis	Novartis
Phase III	Spain	Novartis	Novartis
Phase III	Switzerland	Novartis	Novartis
Phase III	Europe	Novartis	Novartis
Phase III	United Kingdom	Novartis	Novartis
Phase II	Japan	Novartis	Novartis

**Preparation and Method of Delivery**

Oral (All): once-daily

**Indication**

Prevention of acute rejection and graft loss in kidney transplant patients

**Status Comment**

Development for transplantation has been terminated, reason undisclosed (co SEC 20-F, 1/2006). Phase III primary endpoint of non-inferiority narrowly missed; FDA has requested Novartis to conduct a safety analysis of drug's transplantation database (co web, as of 6/2005). NDA submission had been predicted for Q1:2006. European submission planned for Q1:2006 (co web, as of 1/2005).

**Status**

<b>Phase</b>	<b>Region</b>	<b>Developer(s)</b>	<b>Marketer(s)</b>
Discontinued - III	USA	Novartis	Novartis

**Preparation and Method of Delivery**

Oral (All): once-daily

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