



## The Party Continues for MS Drug Companies

### Double Digit Price Increases in 2009 Pay Off

#### Companies:

**Novartis** (NVS)  
**Merck Serono** (Germany: MRCG)  
**Biogen Idec** (BIIB)  
**Teva** (TEVA)  
**Bayer Schering** (Frankfurt: SCH)  
**Élan** (ELN)  
**UCB** (Brussels: UCB)  
**PDL BioPharma** (PDLI)  
**Acorda Therapeutics** (ACOR)

#### Approved Products:

**Avonex** (Biogen Idec)  
**Rebif** (Merck Serono)  
**Betaseron** (Bayer Schering)  
**Copaxone** (Teva)  
**Novantrone** (Merck Serono)  
**Tysabri** (Biogen Idec & Élan)  
**Ampyra** (Acorda Therapeutics and Biogen Idec)  
**Extavia** (Novartis and Bayer Schering)

#### Developmental Products:

**Fingolimod** (NDA submitted, Novartis)  
**Cladribine** (NDA submitted, Merck Serono)  
**Laquinimod** (phase III, Teva)  
**BG-12** (phase III, Biogen Idec)  
**Campath** (phase III, Genzyme)  
**PEG-interferon beta-1a** (phase III, Biogen Idec)  
**Rituxan** (phase II/III, Biogen Idec & Roche)  
**Daclizumab** (phase II, PDL & Biogen Idec)

- Based on better than expected sales for the full year 2009, *inThought* is modestly increasing 2010 worldwide revenue projections, in multiple sclerosis (MS), for Biogen Idec (BIIB) and Élan's (ELN) Tysabri from \$1,075 million to \$1,127 million. 2017 worldwide revenue reaches \$1,502 million in our model.
- Other marketed MS therapies - Avonex (Biogen Idec; BIIB), Rebif (Merck Serono; Germany: MRCG), Betaseron (Bayer Schering; Frankfurt: SCH), and Copaxone (Teva; TEVA) - also performed well in 2009, more because of large price increases than expansion of the market.
- While oral agents would be more convenient than available therapies, use of Novartis' (NVS) fingolimod and Merck Serono's cladribine will be limited by their adversity profiles.
- The recent launch of Extavia, Novartis' rebranded version of Bayer's Betaseron, and the approval of Acorda's (ACOR) Ampyra (fampridine), will not significantly alter the MS landscape.
- *inThought* projects flattening sales of Avonex, Rebif, Betaseron, and Copaxone as biosimilars enter the market and rabid price increases abate. Total revenue from the currently marketed agents will drop from \$9.9 billion in 2009 to \$5.2 billion by 2017.

In our April 15, 2009 report, *Multiple Sclerosis Revenue Model: Increasing Competition from Oral Agents and New Injectibles*, and our August 3 2009 report, *Tysabri Sales Strong, But Challenges Remain: Adjusting MS Revenue Forecasts*, inThought outlined revenue projections for the currently available MS agents and nine agents in clinical development for MS. We now update our model to incorporate actual 2009 reported sales of Avonex, Rebif, Copaxone, Betaseron, and Tysabri.

### The Interferons and Copaxone

Our revenues estimates for Avonex, Betaseron, Copaxone, and Rebif (the ABCRs) change only modestly. Merck Serono's Rebif outperformed our expectations in 2009, and Teva's Copaxone delivered especially impressive results.

The increased U.S. revenue from Copaxone was driven by a 21% increase in price and a 10% increase in patients treated. Increased revenue for Rebif was due to a 15% increase in both cost and patients treated. The other interferons also had large price increases, although the absolute number of patients treated in the U.S. went down. The ABCRs now cost close to \$20,000 per patient per year in the U.S. (Table 1).

The double-digit year-over-year price increases for the ABCRs in the U.S. are unlikely to continue. Even without healthcare reform in the U.S., inThought expects that MS drugs are becoming significant to the bottom line of U.S. payors, who will be more aggressive about stopping future price increases. MS drug makers also take on headline risk for every price increase in an increasingly price sensitive market.

In the absence of large price increases, our model shows flattening growth for the ABCRs in 2010, and a slow decline in revenue starting in 2011. We anticipate that competition from novel agents and pricing pressure from biosimilars will impact revenue from these drugs. Figures 1 and 2 detail the U.S. and worldwide revenue outlook for these agents.

### Tysabri

Worldwide sales for Tysabri were \$1,059 million in 2009, slightly ahead of our previous estimate of \$993 million. At the end of December 2009, approximately 48,800 patients were on Tysabri therapy worldwide.

Despite outperforming our expectations for the year, we remain conservative in our projections of Tysabri revenue growth. Recent updates to the agent's label by the FDA and EMEA reflect the more properly defined risk of developing progressive multifocal leukoencephalopathy (PML). The 31 confirmed cases of PML in patients taking Tysabri (as of January 21) have led to increased caution among prescribers and patients alike. Given this, we anticipate that while more patients will be treated with the agent, the average price per user will decline as patients begin to rotate off therapy more quickly.

We are modestly increasing our 2010-2013 sales estimates for Tysabri, but leaving 2014-2016 unchanged. We forecast worldwide Tysabri sales of \$1,127 million this year, increasing to only \$1.5 billion by 2017 (Figures 1 and 2).

The outlook for Tysabri continues to depend on its evolving adversity profile and, more importantly, whether earlier PML diagnosis and monitoring programs can improve its risk:benefit profile. Additionally, approval of oral MS agents will be a competitive threat more so to Tysabri than to other approved MS drugs.

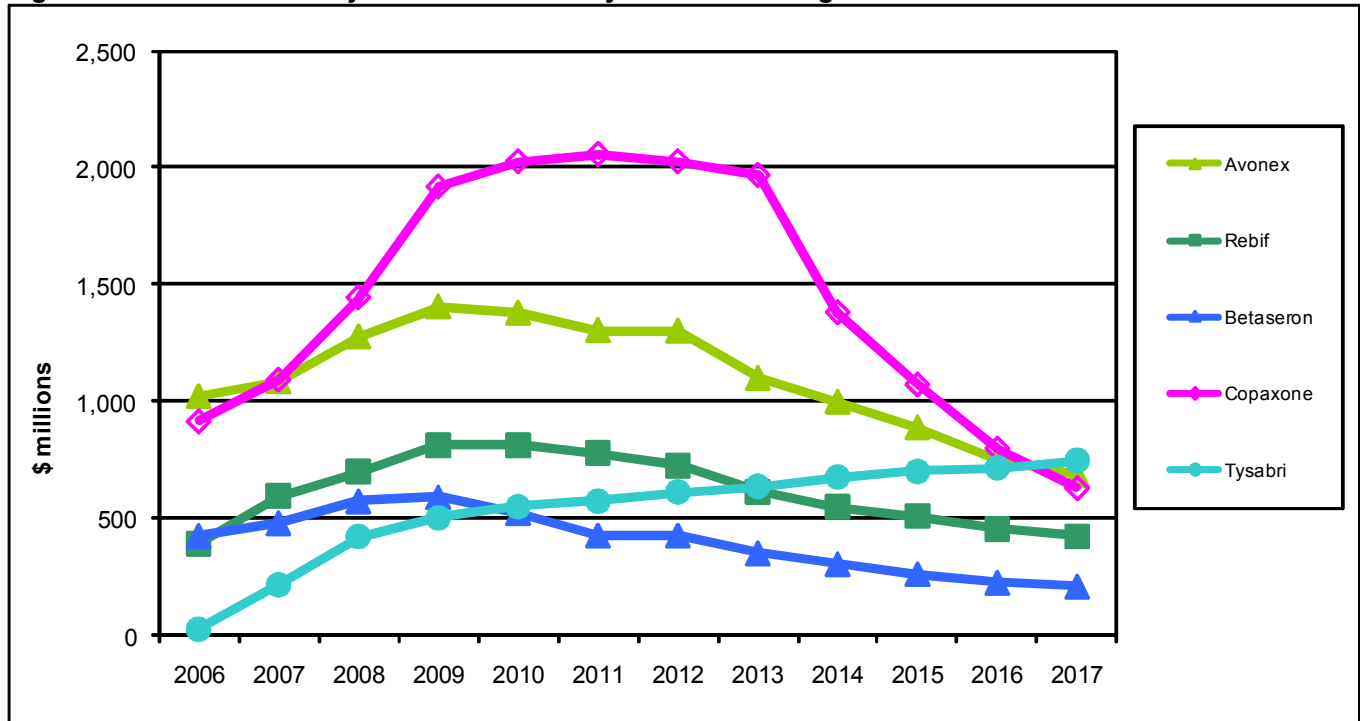
Each of the ABCRs now cost close to \$20,000 per patient per year in the U.S.

**Table 1: Pricing Estimates for the ABCRs**

Drug Name	Developer(s)	2009 Wholesale Acquisition Cost (WAC)	Percent Increase from 2008	2010 Estimated average cost per patient per year
Avonex (IFNβ-1a)	Biogen Idec	\$2,386	18%	\$19,597
Rebif (IFNβ-1a)	Merck Serono	\$2,408	15%	\$19,738
Betaseron (INFβ-1b)	Bayer Schering	\$2,359	18%	\$21,317
Copaxone (glatiramer)	Teva	\$2,392	21%	\$21,460

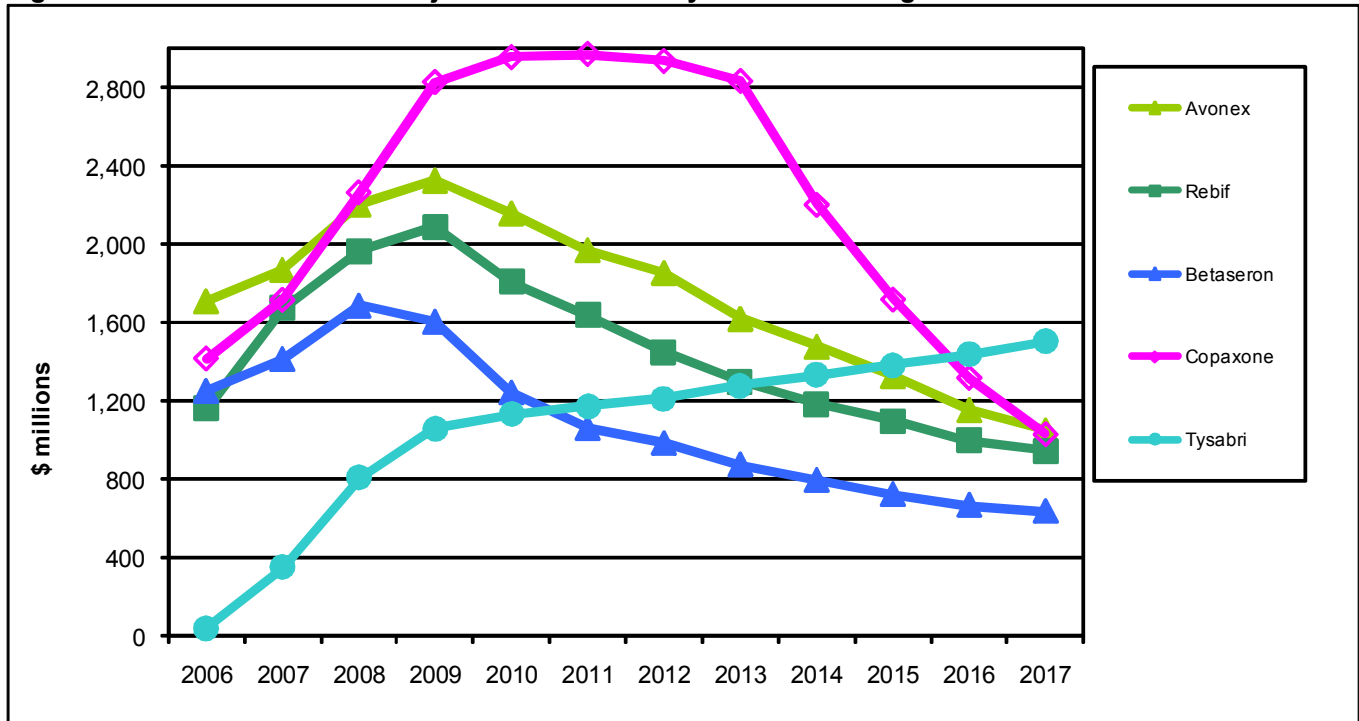
Source: Wolters Kluwer PriceRx and inThought estimates.

**Figure 1: U.S. Revenue Projections for Currently Marketed MS Agents**



Source: Company reports, R&D Insight, Clinical Trials Insight, and inThought estimates.

Figure 2: Worldwide Revenue Projections for Currently Marketed MS Agents



Source: Company reports, R&D Insight, Clinical Trials Insight, and inThought estimates.

### The Oral Agents

Our outlook for Merck Serono’s oral cladribine and Novartis’s fingolimod remain unchanged since our December 2, 2009 report: *Cladribine Delay: Minimal Impact on Fingolimod and Tysabri.*

We continue to believe that while oral agents would be more convenient than available MS therapies, they are unlikely to see significant first-line use. These agents will be the drugs of choice for MS patients looking to either supplement interferon therapy, or those for whom interferon therapy has failed.

Assuming approval for each individual agent, we model 2017 U.S. revenue of \$537 million for Novartis’s fingolimod, \$126 million for Merck Serono’s cladribine, \$192 million for Teva’s laquinimod and \$215 million for Biogen Idec’s BG-12 (panaclar; Table 2, Figure 3 and 4).

### The New Entrants

The recent approval of Acorda’s (ACOR) fampridine, to be branded as Ampyra, does not change our outlook for other MS drugs. We anticipate a tepid reaction from neurologists to use of Ampyra. Our 2017 revenue projection is \$171 million for U.S. sales.

Novartis’ Extavia is an addition to an already crowded market that lacks clinical differentiation. Extavia will face stiff competition from existing agents as well as those in development. While selling Extavia will allow Novartis to build an MS sales force in anticipation the launch of fingolimod, it does not change our outlook for the other agents.

Weekly prescription data from Wolters Kluwer Healthcare Analytics indicates a slow launch for Extavia, with only 125 new patients starts in since launch in the U.S. Use in these patients translates into \$313,000 NRx Dollars.

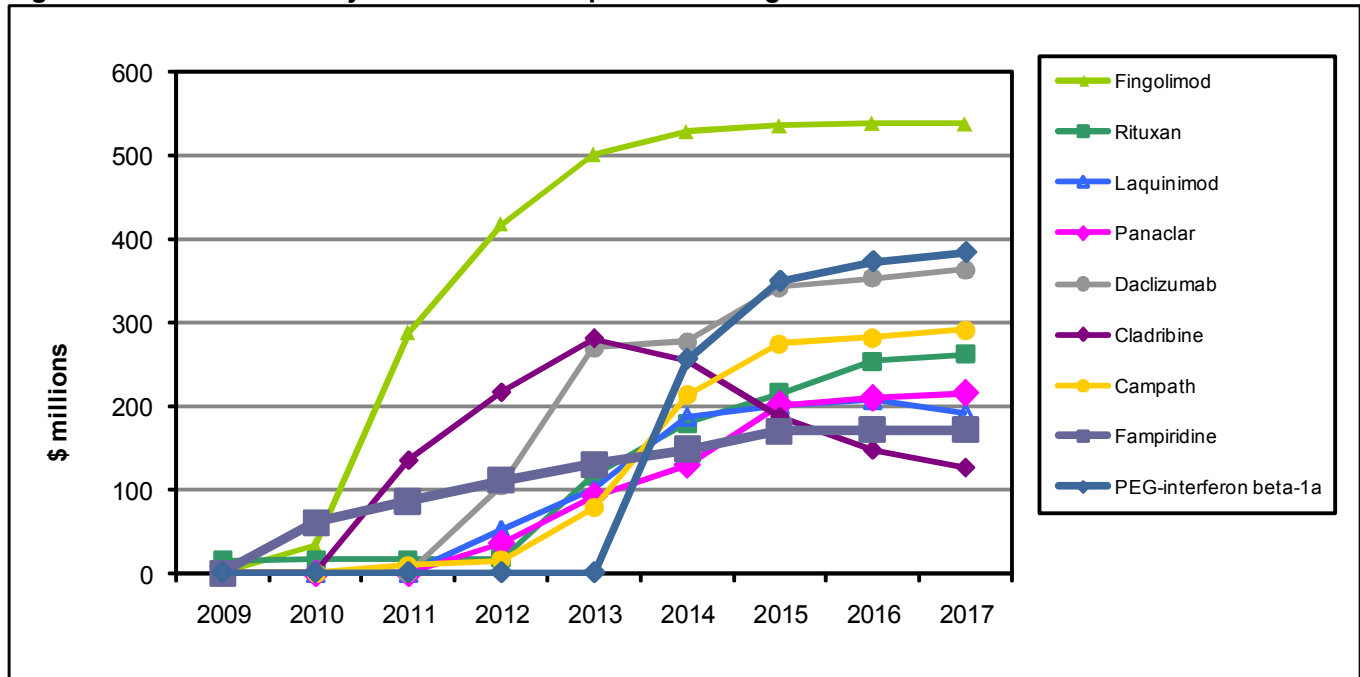
Table 2: Promising Oral MS Agents in Development

Drug Name	Developer(s)	IAI*	Estimated U.S. Approval	2017 U.S. Revenue (millions)	2017 Worldwide Revenue (millions)
Fingolimod	Novartis	62%(B)	Oct, 2010	\$537	\$784
Cladribine	Merck Serono	70% (C)	Jan, 2011	\$126	\$323
Laquinimod	Teva	45% (C)	Oct, 2012	\$192	\$260
BG-12 (Panaclar)	Biogen Idec	50% (C)	Jul, 2012	\$215	\$373

Source: Company reports, R&D Insight, Clinical Trials Insight, and inThought estimates.

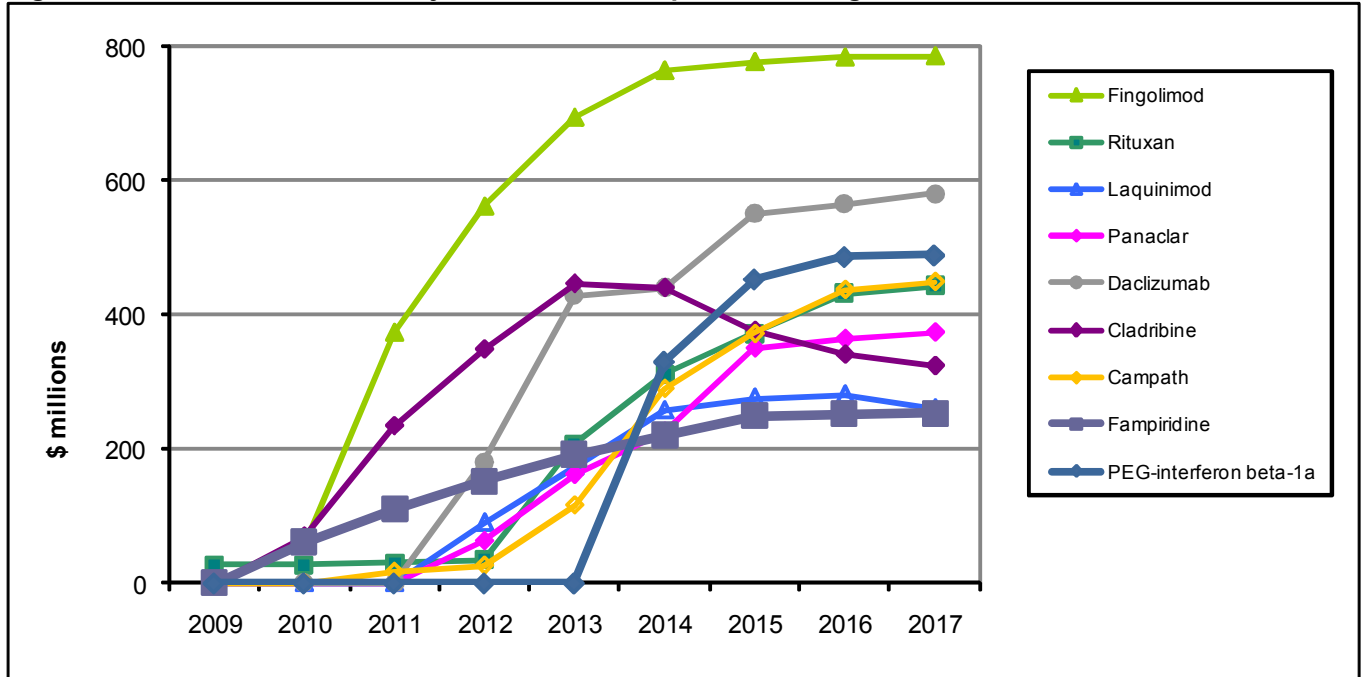
\* IAI = inThought Health Approvability Index (probability of approval)

Figure 3: U.S. Revenue Projections for Developmental MS Agents



Source: Company reports, R&D Insight, Clinical Trials Insight, and inThought estimates.

Figure 4: Worldwide Revenue Projections for Developmental MS Agents



Source: Company reports, R&D Insight, Clinical Trials Insight, and inThought estimates.

### inThought Revenue Forecasts

inThought revenue forecasts employ a proprietary model developed to assess both currently approved and developmental drugs as well as medical devices. Models are developed for a given therapeutic area using a “top-down” approach based on the addressable patient population, allowing for detailed assessment of a compound’s real or potential competitive landscapes. Epidemiological considerations include estimates of disease incidence, prevalence, growth rates, and death rates. Models are developed separately for the U.S., Europe, and Japan. inThought drug revenue models look seven years into the future and three years into the past; device revenue models project three to five years forward and three years back. For developmental agents, the revenue forecast assumes the drug or device is approved. Risk adjusted valuations can be developed by multiplying the revenue potential, if approved, by the probability of approval as assessed by the inThought Approvability Index.

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