



Gilenya Highly Anticipated, but Uptake Will be Slow

Results from a Survey of U.S. Neurologists

Companies:

Novartis (NVS)

Merck Serono (Germany:
MRCG)

Biogen Idec (BIIB)

Teva (TEVA)

Bayer Schering (Frankfurt:
SCH)

Élan (ELN)

Acorda Therapeutics (ACOR)

Products:

Gilenya (Novartis)

Avonex (Biogen Idec)

Rebif (Merck Serono)

Betaseron (Bayer Schering)

Copaxone (Teva)

Tysabri (Biogen Idec & Élan)

Ampyra (Acorda Therapeutics
and Biogen Idec)

Extavia (Novartis and Bayer
Schering)

- *inThought* and ImpactRx surveyed 76 U.S. neurologists to gauge the real-world impact of Novartis's (NVS) recently approved oral multiple sclerosis therapy Gilenya (fingolimod).
- Nearly all respondents were familiar with Gilenya. Nine have already prescribed it, and over half are planning to prescribe it by the end of the year.
- Respondents expect that over 20% of their multiple sclerosis (MS) patients will use Gilenya over the next two years.
- However, the neurologists were overwhelmingly cautious about Gilenya's safety profile, anticipating that first-line use (prior to interferons or Copaxone) is not appropriate. Respondents indicate that Gilenya will be appropriate for 14% of MS patients as first-line use, compared to 42% of patients poorly controlled by interferons or Copaxone.
- The results of the survey are consistent with feedback from the ECTRIMS meeting that Gilenya will not replace interferons and Copaxone as first-line therapy until its safety profile is better defined. We are reiterating our 2017 worldwide sales estimate of \$1.5 billion.
- Respondents also commented on current use of Biogen Idec (BIIB) and Élan's (ELN) Tysabri, Acorda's (ACOR) Ampyra, and other MS agents, as well as on their anticipation for developmental MS therapies.

ImpactRx (www.impactrx.com) fielded an internet-based survey written by inThought, with responses from 76 practicing U.S. neurologists who each see at least 5 multiple sclerosis (MS) patients per month. Most respondents have a private practice, while 15 practice at a community or academic hospital setting. The average number of MS patients seen per month is 44, with 90% of those currently using pharmacotherapy for their MS treatment. Current therapies included:

Avonex	24%
Rebif	19%
Betaseron	15%
Extavia	1.8%
Copaxone	32%
Tysabri	5.1%
Ampyra	7.3%
Rituxan	0.8%

Nearly all were aware of Novartis's Gilenya. On a five point scale, 16 of 76 neurologists were "very familiar" with Gilenya, 29 were "quite familiar," 28 were "somewhat familiar" while only 3 were "somewhat unfamiliar." None were "completely unfamiliar."

Anticipated Use of Gilenya

Similar to sentiment at last month's European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) conference in Göteborg, Sweden, we found that respondents were hesitant about substituting Gilenya for interferons or Copaxone as first-line therapy for MS. The best candidates for Gilenya are, "Patients who are poorly controlled by interferons and Copaxone" followed by "Patients who are currently using interferons or Copaxone that would like to try an oral medicine", then "Patients who are currently using or have used Tysabri." The lowest rated category is, "Relapsing remitting MS patients who have not previously used an interferon or Copaxone."

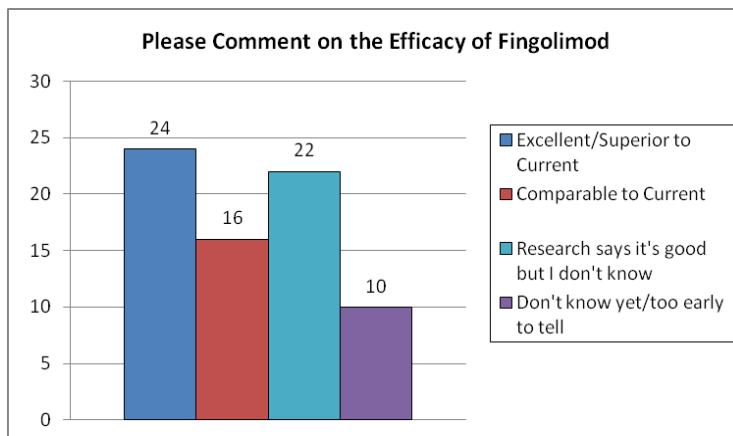
Interestingly, those 16 rating themselves as very familiar with Gilenya considered first-line use even less appropriate than those less familiar with the drug. Those 16 physicians, however, are more likely to prescribe Gilenya to poorly controlled patients and Tysabri patients.

Anticipation for use of Gilenya is strong, although respondents will not adopt first-line use immediately. On average, the respondents expect to prescribe Gilenya to 9% of their MS patients over the next 6 months, and to 23% of their MS patients over the next 2 years. Nine have already prescribed Gilenya, with 5 more expecting to do so this month. Half of the rest of the doctors will prescribe Gilenya this year, with the rest likely waiting until 2011 and only one not expecting to prescribe it at all. The percentage of each patient group expected to receive Gilenya over the next six months is described in the chart below:

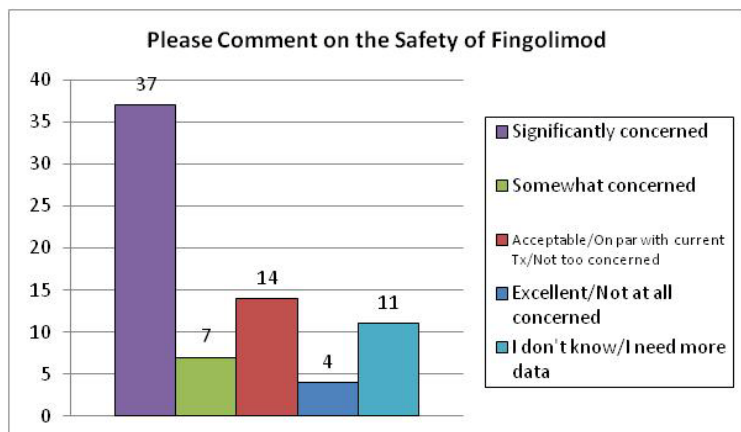
Relapsing remitting MS patients who have not previously used an interferon or Copaxone.	14%
Patients who are currently using interferons or Copaxone that would like to try an oral medicine.	23%
Patients who are poorly controlled by interferons and Copaxone.	42%
Patients who are currently using or have used Tysabri.	14%

Safety and Efficacy

The efficacy of Gilenya is well accepted by our respondents. The 73 neurologists who were at least "somewhat familiar" with Gilenya gave the following responses regarding the efficacy of Gilenya (fingolimod).



Safety of Gilenya, however, is of significantly greater concern:



In an open ended format, concerns cited included cardiac issues (n=19), macular edema (15), infections (15), and malignancies (10). Uncertainty about the safety profile is a key issue for many with eleven respondents stating the critical need for longer terms safety data. Typical comments include:

"Not sure. Appears to be too immunosuppressive"

"A little better than Tysabri"

"Concerns about assorted monitoring issues"

"Concerns exist re opportunistic infections and neoplasms"

"Worried about the unknowns"

"Unclear-cardiac problem makes it a little hard to start-disseminated herpes is concerning"

"Measures in place for bradycardia, wbc, liver, eye, cancer possibilities"

"Strong safety issues"

"Need to wait to see lone term safety data"

"Too early to say; needs to have longer time of use and larger number of patients to say" "Risky"

"Really quite safe"

"Scuttlebutt points to some major potential side-effects."

Overall Impressions of Gilenya

The majority of respondents believe that Gilenya will have a significant impact on the care of MS so long as safety remains acceptable and patient assistance programs are implemented. High cost was cited by many respondents as a possible impediment to optimal use, although there was little consensus on the impact of the cost of Gilenya on its eventual use.

In spite of the overall excitement about Gilenya's potential, a significant number of neurologists expressed hesitation about prescribing the drug until its safety profile is better defined:

"Scary stuff - I don't want to be sued for skin cancer or cardiac complications."

"Effective, but safety concerns, and tedious to start. I'm also concerned about our liability when it comes to 'monitoring' patients after their first dose."

"Too demanding"

"More effective than current injectables, but less than Tysabri. Also, intermediate risks."

"Very efficacious, prescribing pre-eval cumbersome and expensive, reasonable safety"

"Very promising more convenient. Will improve quality of life"

"Fairly positive, again somewhere between the ABCR drugs and Tysabri."

"Thus far it is very good. I think only time will tell"

"Scary"

"Effective but not safe"

"Seems effective but risky."

"Not a great impression; it is outrageously expensive for an oral medication and it is not even as effective as Tysabri"

"Not excited to prescribe at this time"

"Have safety concerns which will not allow me to use it first line"

Tysabri and the MS Pipeline

Respondents have not significantly changed their degree of Tysabri use over the last year, nor have they changed the average duration of Tysabri therapy for a typical MS patient. Anticipation for a JC virus assay to help limit the risk of PML is muted, with most indicating that such a test would either modestly increase their use of Tysabri (n=38) or have no impact (n=24).

Looking forward to new agents, in an open ended format, 24 respondents mentioned as promising cladribine, 14 cited laquinimod, 13 Campath, 9 BG-12, and 6 each mentioned Rituxan and teriflunomide.

Changes to MS Revenue Model

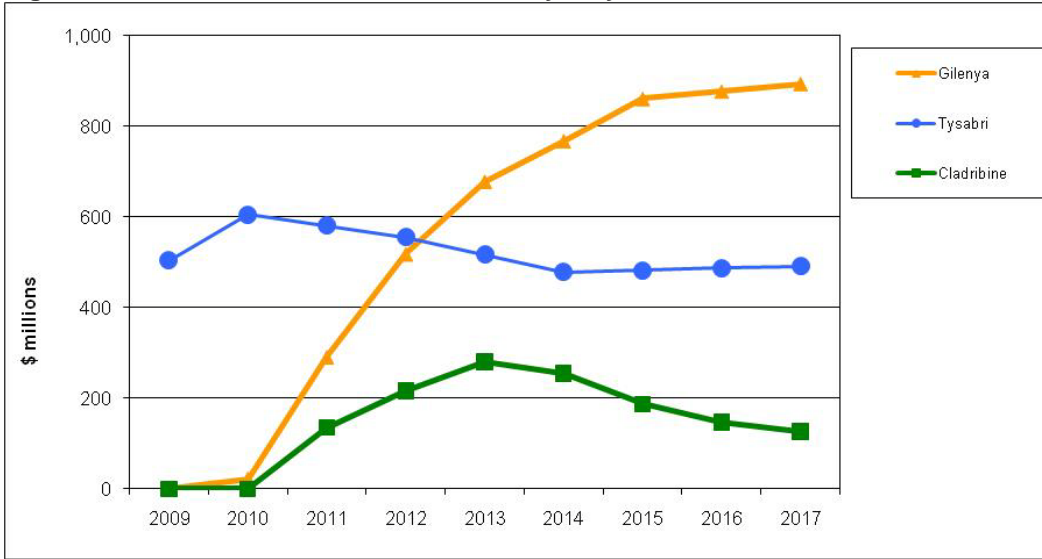
The results of the survey are largely consistent with our previous analysis of Gilenya and other MS therapies on the market and in development. Anticipation for Gilenya is high, but eventual use will depend on the real-world safety profile observed over the next two years. We are therefore reiterating our long-term revenue estimates for Gilenya in the U.S. or worldwide, with remain \$900 million in the U.S. and \$1.5 billion worldwide in 2017.

However, we are slowing the ramp to those 2017 numbers somewhat given the hesitation to prescribe Gilenya in a first-line setting shown by our respondents as well as the concerns about price holding back sales. The updated revenue projections for Gilenya compared to Tysabri and cladribine are shown in the figures on the next page.

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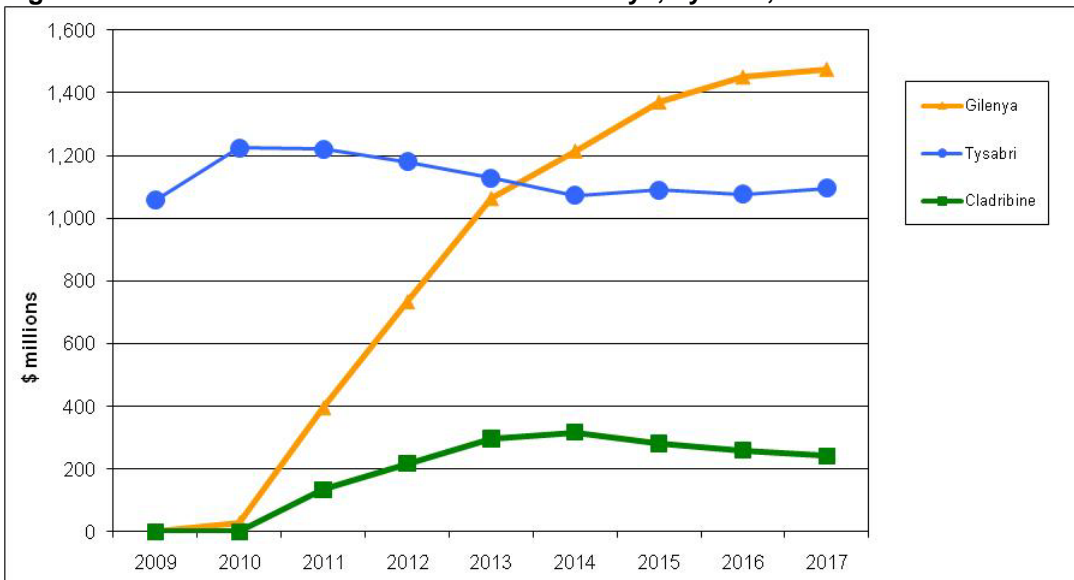
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Figure 3: U.S. Revenue Forecasts for Gilenya, Tysabri, and Cladribine.



Source: inThought estimates, company data

Figure 4: Worldwide Revenue Forecasts for Gilenya, Tysabri, and Cladribine.



Source: inThought estimates, company data