12 December 2013
Americas/United States
Equity Research
Biotechnology (Biotechnology (US)/Biotechnology & Biopharmaceuticals (Europe)) / MARKET WEIGHT

Multiple Sclerosis: It's a Revolution! (vs. Evolution)

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COMMENT

NIMOs are winning the revolution; Generics could complicate

Summary: On Dec 10, TEVA held a FY 2014 guidance investor call. During the call, TEVA management gave notable granularity (especially with regards to patient numbers) on the MS market and outlined scenarios with and without 2014 generic Copaxone entry (Exhibits 1-4). The incremental data from the call has important read-throughs to all players in the MS space and allowed us to check our assumptions in our previously published patient-based global MS market model (LINK#1, LINK#2). In this note, we outline our observations/implications from the TEVA call, especially on read-throughs to next-gen oral MS agents.

- **TEVA (implicitly) estimates that orals will capture ~33% patient share in the U.S. in 2014 – Bigger than our/Street's estimates!** TEVA commented during the Q&A session that they anticipate that >100K patients in the U.S. could be on Orals by the end of 2014. This number represents meaningful upside to our/Street's current estimates. Our model estimates that in 2014 in US ~295K patients will be on a MS drug, of which ~25% (~70K) will be on Orals. As TEVA acknowledged during the call, ABCRs will be losing patients to the Orals. Specifically, TEVA estimated/implied that Copaxone (which they confirmed as having ~85K patients on treatment – bang in-line with our model estimates, 84.9K) could lose ~15K patients ($500M) to Orals in 2014 in the US (i.e. a **20% per annum "Copaxone to oral switch rate"**).
- **TEVA assumes significant generic substitution of branded Copaxone.** Under the generic Copaxone scenario, TEVA assumes that there will be two AB-rated generics launched in June 2014. Within a half-year of this launch, TEVA expects ~25% of branded Copaxone 2013 patients to switch to generic Copaxone. On a full year basis, this translates into ~50% of branded patients will be on generic Copaxone. TEVA is essentially modeling a "relatively" normal AB-rated generic market for Copaxone in the medium to long term – this is in line with our modeling (we estimate $445M US branded Copaxone revenues in 2017).
- **Strong uptake of Tecfidera is anticipated in Ex-US.** TEVA acknowledged that Tecfidera could capture ~5% market share in Ex-US by the end of 2014. As a point of reference, we currently assume ~2.5% patient share for Tecfidera in the Ex-US (CSe Tecfidera ROW estimate for 2014 = $295).
- **High initial Copaxone 40mg/TIW switching (from 20mg/QD) expected – why not more ultimately**? TEVA disclosed that it plans to price Copaxone TIW (expected launch in Feb 2014) "more or less" at par with Copaxone QD. TEVA also guided that (either with or without generic Copaxone) Copaxone 40mg/TIW is expected to capture ~40K patients (i.e. 50% of 2013 base) by year end (with ~30K by Jun 2014).

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- **Read-through to "next-gen" agents – Oral differentiation is a key near-term issue.** Clearly, there are a number of key variables left to play out with regards to generic Copaxone (including pricing, speed of pricing erosion, AB-rated substitution, number of players, ROW situation, potential TEVA authorized generic), but the macro/medium term take-home is clear in our view: Generics of Copaxone (and for that matter interferons) will happen, placing a headwind on branded players in the MS space especially the Orals. In our view, the ability of next-gen agents to show/reinforce differentiation either clinically or via convenience will be key to defending against generic ABCRs.

Exhibit 1: **Key Figures from TEVA FY'14 Guidance Call**

	Exclusive Copaxone	Generic Copaxone
Assumption	No generic Copaxone in US (or ROW) in 2014. Assumes 40/mg TIW Copaxone launched Feb 2014.	FDA allows generic Copaxone in US starting in June 2014. ROW Copaxone protected until May 2015. Assumes 40/mg TIW Copaxone launched Feb 2014.
Teva Guided WW Copaxone Sales	$3.6B to $3.7B WW (FY13 CSe = $4.0B WW, US$2.9B, ROW $1.1B)	$3.1B to $3.2B
Loss in Copaxone Sales	~$500M ("mainly due to intensified oral competition, main in the US")	~$500M (due to orals) ~$600M ("assuming "two generic competitors will launch AB-rated generic version…in June '14")
Treated Patients (Teva confirmed 85K Copaxone patients in US currently)	Copaxone QD: ~31K Copaxone TIW: ~40K by year end (~30K by June 14) Orals: ~14K	Copaxone QD: ~11K by year end Copaxone TIW : ~40K by year end (~30K by June 14) Generic Copaxone: ~20K by year end CS calculated implication is orals capture remaining ~14K
Ex-US Market Share		Tecfidera: 5%

Source: Teva, Credit Suisse research

Exhibit 2: **TEVA Comments on MS Market during FY'14 Guidance Conference Call**

	Exclusive Copaxone	Generic Copaxone
Assumptions	"The first scenario or the exclusive Copaxone scenario assumes no generic competition to Copaxone in 2014 and is expected to reduce our operating profit by $500 million due to oral competition."	"The second scenario or the generic Copaxone scenario assume generic competition to Copaxone in the U.S. as early as June 1, 2014, in the form of two AB-rated competitors…This represents a total reduction of Copaxone net profit of approximately $1 billion from anticipated 2013 level."
Guided WW Sales in 2014	$3.6B to $3.7B	$3.1B to $3.2B
Patients on Copaxone 20mg (QD) in the US in 2013	"Today in Copaxone we are having about 85,000 patients in total. We expect that and we see that in the last quarter we've lost about 5% in terms of that to the orals."	"Today in Copaxone we are having about 85,000 patients in total. We expect that and we see that in the last quarter we've lost about 5% in terms of that to the orals.
Loss on Copaxone Sales in 2014	"In the Exclusive Copaxone scenario, Copaxone revenues in 2014 are expected to decline by approximately $500 million from 2013. This decline in revenues over 2013 is mainly caused by the intensified oral competition, mainly in the U.S."	"In the Generic Copaxone scenario, Copaxone revenues in 2014 are expected to decline by about $1.1 billion from 2013. This scenario assumes that two generic competitors will launch an AB-rated generic version of Copaxone 20-milligram in the United States in June, 2014…"
Patients on Copaxone 20mg (QD) in the US in 2014	"In the scenario where we have no generic competition, we still should have well over 70,000 patients on Copaxone."	"… while Teva Copaxone 20-milligram would have approximately 11,000 patients at the same mark [end of 2014]…"
Patients on Copaxone 40mg (TIW) in the US in 2014	"Again, this scenario assumes Copaxone 40-milligram is launched in the U.S. by February 2014 with approximately 30,000 patients by the end of May, rising to 40,000 patients by the end of the year."	"In addition, we expect to launch Copaxone 40-milligram in the U.S. by February 2014 with approximately 30,000 patients by the end of May 2014, rising to more than 40,000 patients by year-end." "…we really expect that when we launch in February by the time of say June we will have 30,000 patients on Copaxone 40. Year-end it's going to be over 40,000 on that Copaxone 40 three-times-a-week."
Patients on Generic Copaxone in the US in 2014	- - - - -	"… which by year-end would capture approximately 20,000 patients…at the same mark [end of 2014]." "We expect that if they launch in June of 2014 that about 25% of the Copaxone will go to a generic, and – but we also expect that the conversion to the three times weekly 40 will continue. So in essence, if you look at that by year-end they should be around 20,000 patients, that's our assumption in this plan, of 20,000 patients will be on a generic Copaxone if and when they make it to the market, which is far from certain."
Patients on Oral Therapies in the US in 2014	"We are still very much the leader both in new prescription and in total prescription for Copaxone, but still expect for next year that the orals continue to make an inroad in the U.S. And we expect that patient numbers of the orals probably to go up, not only at the cost of Copaxone. They will – I think we'll probably see more of interferon beta that will switch to Copaxone, but still we expect that the orals will be above 100,000 at the end of 2014."	"We are still very much the leader both in new prescription and in total prescription for Copaxone, but still expect for next year that the orals continue to make an inroad in the U.S. And we expect that patient numbers of the orals probably to go up, not only at the cost of Copaxone. They will – I think we'll probably see more of interferon beta that will switch to Copaxone, but still we expect that the orals will be above 100,000 at the end of 2014."

Source: Teva, Credit Suisse research

Exhibit 3: **TEVA Comments on MS Market during FY'14 Guidance Conference Call (continued)**

	Exclusive Copaxone	Generic Copaxone
Copaxone Authorized Generic	"In terms of launching an authorized generic, we continue to monitor that carefully and frankly I'm also not willing to disclose our commercial strategy on that. At the moment we believe that Copaxone is such an important product that this is definitely something that first and foremost we hope to defend Copaxone itself as a brand."	"In terms of launching an authorized generic, we continue to monitor that carefully and frankly I'm also not willing to disclose our commercial strategy on that. At the moment we believe that Copaxone is such an important product that this is definitely something that first and foremost we hope to defend Copaxone itself as a brand."
Potential Number of Copaxone Generics	- - - - -	"Well, the planning is that if there's generics, there will be two, but we are aware of a third ANDA filed for sure and a fourth one potentially there. So there's – there could be multiple, but the evidence is still there that we really believe there should be – and we have very good scientific reason to believe this, clinical data from patients right so whether this happens or not, remains to be seen, but at the moment, there's more than two ANDA filings in the U.S."
Price for Copaxone 40mg TIW	"We already said that in the pricing assumptions in the past we are assuming more or less [par] pricing, but I really don't want to go too much into competitive information on that."	"We already said that in the pricing assumptions in the past we are assuming more or less [par] pricing, but I really don't want to go too much into competitive information on that."
Copaxone in Ex-US in 2013	"The Copaxone in Europe's actually doing fairly well. We're seeing at the moment an increased number of patients, low single digit but still an increase. Ever since we've taken over the product back from Sanofi it's really extremely – we are very happy with it, really content with it. In – also in ex-Europe and ex-USA, for instance in Russia we've seen a tender come through. It's always difficult to predict tenders going forward but actually the majority of business of Copaxone really is in the U.S. and then in Europe. And that really makes most of what we're seeing there. Also given by incidence and prevalence of the disease actually, this geographical parts."	"The Copaxone in Europe's actually doing fairly well. We're seeing at the moment an increased number of patients, low single digit but still an increase. Ever since we've taken over the product back from Sanofi it's really extremely – we are very happy with it, really content with it. In – also in ex-Europe and ex-USA, for instance in Russia we've seen a tender come through. It's always difficult to predict tenders going forward but actually the majority of business of Copaxone really is in the U.S. and then in Europe. And that really makes most of what we're seeing there. Also given by incidence and prevalence of the disease actually, this geographical parts."
Copaxone in Ex-US in 2014	"For next year going forward, we expect that Copaxone will get a little bit more headwind of the competition in Europe, although the rollout of a new product is always slower than what you typically see in the U.S. because of the need to get prices and reimbursement in single countries approved. So with the current performance and strong adherence to Copaxone, this is basically – we're not expecting too much of an impact outside of the U.S. actually and keep more or less the same sales levels."	"For next year going forward, we expect that Copaxone will get a little bit more headwind of the competition in Europe, although the rollout of a new product is always slower than what you typically see in the U.S. because of the need to get prices and reimbursement in single countries approved. So with the current performance and strong adherence to Copaxone, this is basically – we're not expecting too much of an impact outside of the U.S. actually and keep more or less the same sales levels."
Tecfidera in Ex-US in 2014	"But for next year we expect more or less 5% of our patients to – we expect Tecfidera to take about a 5% market share at year-end of 2014. And that's what we've factored in. And that's probably the major point in the entire competition."	"But for next year we expect more or less 5% of our patients to – we expect Tecfidera to take about a 5% market share at year-end of 2014. And that's what we've factored in. And that's probably the major point in the entire competition."

Source: Teva, Credit Suisse research

Exhibit 4: **TEVA Comments on MS Market during FY'14 Guidance Conference Call (continued)**

	Exclusive Copaxone	Generic Copaxone
Enthusiasm for Copaxone 40mg TIW	"So on the 40-milligram, why we are quite optimistic is actually because we do extensive market research with both payers, patients and physicians and we see an increased enthusiasm for this product. It's a product that will have the same safety and efficacy and everything that people have come to appreciate for Copaxone 20 but give that at a 60% lower injection frequency so that people start to really see this as a very important and valuable product for them to get to market and based on that, we believe that we will be definitely seeing very good uptake of that product when we get it registered, which should happen at the end of January, 2014. And we really believe that the product will even do better than in our initial assumptions of 30% to 50% uptake, we believe it might even do better than that."	"So on the 40-milligram, why we are quite optimistic is actually because we do extensive market research with both payers, patients and physicians and we see an increased enthusiasm for this product. It's a product that will have the same safety and efficacy and everything that people have come to appreciate for Copaxone 20 but give that at a 60% lower injection frequency so that people start to really see this as a very important and valuable product for them to get to market and based on that, we believe that we will be definitely seeing very good uptake of that product when we get it registered, which should happen at the end of January, 2014. And we really believe that the product will even do better than in our initial assumptions of 30% to 50% uptake, we believe it might even do better than that."
Branded Copaxone vs. Generic Copaxone	- - - - -	"We're, of course, continuing to do our work also to analyze all aspects of Copaxone and have recently published data on Copaxone and also comparison to generic Copaxone. Interestingly there, Copaxone mechanism of action was outlined and documented and evidence provided in terms of gene expression that really paralleled its protective effect in terms of inflammation. But this has raised significant concerns also about the generics that don't appear to have the same activity profile relative to the gene expression profile of Copaxone. And really raised the question about whether they actually have impact not only on the T-cells in a negative way but also raise gene expression for monocytes, which would potentially be pro-inflammatory" "...I think what's really the most important thing we have to do and can do to influence that is to make sure that Copaxone 40 comes to market and support that. The enthusiasm for that product is really something that makes us very optimistic that this will be switching most of the patients that currently use Copaxone 20 to 40, which has a patent protection till 2030. So that's a very different ball game in that respect and that is really the most important thing we can do. Second, what we really pick up from all of our market research, that there is a genuine concern on patients and also from doctors on the quality of a generic. The fact that these products have not been tested in man, there are no clinical evidence on safety and efficacy. It really is a concern to them. So I think that will also limit the ability of payers to really influence choices and patients might really opt for something completely different. So what we can, and I doubt that they can overcome that concern with price decreases, they will have to overcome that concern really with data and showing their safety and efficacy, right?" "So for us, the most important thing to do is continue to stay in dialogue, as Michael explained before, on some of the findings that we have, scientific evidences that we have that put questions around the sameness of those so-called generics, and in commercial, medical and every support we can give to make sure the patients get the chance to use the three-times-a-week 40. That really forward going is what we do."

Source: Teva, Credit Suisse research

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