Roche: TDM-1 (Phase III/Breast Cancer) Set to Cannibalize Herceptin Market Given its Superior Adverse Event Profile; Could Price TDM-1 50% Above Herceptin

TDM1 set to quickly cannibalize Herceptin sales in the U.S., driven by phase III data in each of the lines of therapy. Consensus forecasts are for CHF 300 million in 2014E (risk-adjusted). Following discussions with our network of opinion leaders, we believe that **following U.S. approval, many oncologists will quickly gravitate to TDM1 use instead of Herceptin in all lines of HER2 mBC. We anticipate that 40% of Herceptin use is in the metastatic setting.**

First-line and EMILIA data limits downside from current U.S. filing. Our sources are optimistic that the FDA will accept the two phase II filings to secure approval in the refractory setting up a sub Part H protocol. The single-arm open label phase II trials show a partial response for heavily pre-treated patients given TDM1 monotherapy. Importantly, the duration of the responses is impressive at c.4 months. Use in the first- line setting will likely be facilitated by interim phase II analysis from a first-line trial expected to be reported at the ESMO meeting. This trial compares T-DM1, given as a single agent, to Herceptin plus Taxotere. Positive data from this interim analysis should enter the Medicare compendia, facilitating US insurance coverage in the first-line setting. **We anticipate Roche to initiate a front-line TDM1 phase III HER2 mBC trial before year-end.**

The head-to-head EMILIA trial of TDM1 in second line metastatic breast cancer could mature before year-end, possibly in time for the SABC meeting in December 2010. Roche continue to guide towards 2012 for the data from this trial. We anticipate that EMILIA will show that TDM1 alone improves PFS to at least similar level to the current gold standard (Xeloda + Tykerb) but with a significantly improved adverse event rate. Existing clinical experience with TDM1 has shown transient thrombocytopenia and some minor gastro-intestinal disturbance.

Roche can price TDM1 50% above price of Herceptin. Our optimism for premium pricing is based on:

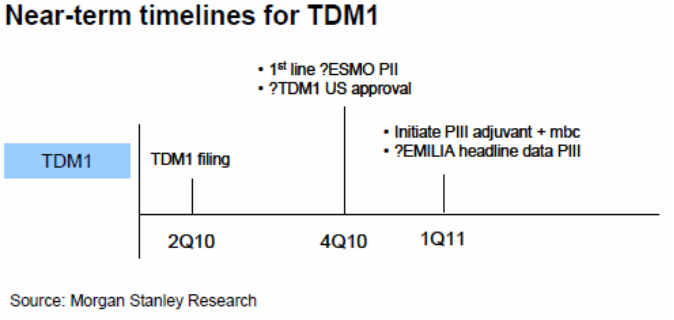
- TDM1 obtaining at least pricing parity with the Xeloda + Tykerb EMILIA regiment on a per month basis.
- Direct cost effectiveness comparisons versus more recently approved biologics for cancer care.
- TDM1 cost effectiveness on a system level making assumptions for lesser supportive care drugs, lesser administration time and lesser adverse events.

We calculate that, assuming c.6 months time to disease progression, the EMILIA second-line regiment of Xeloda +Tykerb costs c. $36,000/treatment in the U.S. market. This would represent a 70% premium to the equivalent duration of Herceptin treatment in the U.S. Importantly, this comparison does not factor in the likely superior safety, better tolerance and potentially superior efficacy data. Separately, given that Herceptin was the first introduced biologic for cancer, its pricing looks positively reasonable compared with some more recent benchmarks like Avastin. We therefore **anticipate TDM1 in the U.S. to be priced at c.$60 000- $65 000 for 12 months therapy (50% premium to Herceptin), with a price cap for low-income patients (as applied to Avastin for breast cancer in the U.S. market).**

Pricing of key cancer treatments

Drug	Manufacturer	Price per month ($)
TDM-1	ROG	5,000-5,400
Tykerb	GSK	3,000-4,300
Afinitor	NOVN	7,330
Gleevec	NOVN	4,593
Tasigna	NOVN	6,832
Nexavar	BAYN	6,661
Revlimid	CELG	485
Sprycel	BMY	5,700
Sutent	PFE	8,715
Tarceva	ROG	4,437

Source: Company data, Morgan Stanley Research



Source: Morgan Stanley/Baum, May 27, 2010
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