Biotech Daily
Marc Sinatra's Bioguide

May 5, 2008

CHEMGENEX REVISITED – THE NEXT BILLION DOLLAR BIOTECH

Introduction: I didn't provide a firm valuation on Chemgenex the last time I reviewed it and this has bothered me since (See Biotech Daily; February 22, 2007). I believe it is the most undervalued biotech on the ASX, a view I have backed with my own money.

Chemgenex is undervalued because the market has underestimated both the likelihood of its lead compound, omacetaxine mepesuccinate (OMA), making it to market and the revenues it can derive in treating chronic myeloid leukaemia (CML) and related diseases.

Why has the market undervalued Chemgenex?

Omacetaxine Mepesuccinate: OMA is a semi-synthetic version of homoharringtonine, a natural alkaloid found in evergreen coniferous shrubs. These shrubs have been used in traditional Chinese medicine to treat leukaemia.

There is a substantial body of published evidence, much of it independent, to indicate that OMA is efficacious in the treatment of CML and related diseases. Importantly, OMA acts at a point downstream to the target of the currently used tyrosine kinase inhibitors (TKIs). This is important because it provides the rationale to support the observation that OMA works in patients resistant to one or more TKIs.

Clinical Trials: OMA is in registration directed phase II/III trials in two CML patient groups:
i) Patients who have failed on the TKI imatinib (Gleevec) and carry a mutation termed T315I (completion expected late 2008).
ii) Patients who have failed on two or more TKI's (completion expected late 2008).
It has orphan status for both groups and, notably, fast track status for the first group.
OMA is also in phase II studies for myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) (completion expected early 2009).

Competitive Landscape: Treatment of CML is dominated by imatinib, with two second line therapies recently approved, dasatinib (Sprycel) and nilotinib (Tasigna). All three are targeted drugs aimed at blocking the anti-apoptotic kinase activity of the BCR-ABL fusion protein, an abnormal protein associated with most cases of CML.

Dasatinib and nilotinib were designed to, and have, overcome resistance to imatinib by binding BCR-ABL in different ways. But all three TKIs are ineffective against the T315I mutation of BCR-ABL, which is why OMA was granted fast track status for this indication. Several other drugs are in development to treat the T315I mutant, all in early stage clinical trials and well behind OMA.

Market Characteristics
Patients: In general, the market size for CML is small with 4,830 people expected to be diagnosed with the disease in the US in 2008. More importantly the prevalence of CML is increasing as imatinib prolongs life. Estimates vary widely, but prevalence in the US of 40,000 – 60,000 seems likely. Resistance in newly treated CML patients arises at a rate of three to five percent a year and 15-20 percent of resistant patients have the T315I mutation. The incidence in the US of T315I has been estimated at 200-500 cases a year.

With respect to the other major markets for OMA, it is estimated that there are 50,000 Americans suffering AML and that 13,290 new cases will be diagnosed in 2008. Where MDS is concerned, the prevalence is thought to be in the order of 30,000 to 40,000 patients, with 10,000-15,000 diagnosed annually.

Prices: Treatment with imatinib costs $US30,000 a year, while dasatinib costs $US45,000 a year. Patients receive treatment for the rest of their lives.

Sizes: Finding market size estimates for OMA's target markets are difficult, but market leader, imatinib, had revenues of $US2.6 billion in 2006. Sprycel was approved by the FDA in mid-2006 and had sales of $US102 million for the first nine months of 2007.

In 2006, Frost and Sullivan estimated the market potential of OMA to be $US336 million for CML, $US396 million for AML and $US630 million for MDS.

Opinion: OMA is not exciting in the traditional scientific breakthrough sense. Unless you look at the independent trials using homoharringtonine, it would be easy to underestimate the chances of OMA making it to market. Also, CML and its related diseases are not well understood by the market. Combined with technical niche indications and low patient numbers, it is a drug that many investors would pass over without much thought.

The alternative to drug therapy, however, is a bone marrow transplant; a procedure that only suits certain patients, has significant safety issues and costs about $US250,000. All of a sudden, $US30,000 or $US40,000 per year for a drug doesn't sound bad. Multiply $US30,000 for annual treatment with OMA by a reasonable estimate of 5000 CML patients worldwide with the T315I mutation and you have a $US150 million market that is wide open and growing.

Next, you need to factor in likely approval for broader use in CML, followed by possible approvals for MDS and AML. If the Frost and Sullivan numbers can be believed, this all adds up to a potential yearly market of $US1.4 billion.

Off label-use and a trend toward combination therapies are likely to cause OMA's sales to increase faster than marketing approvals for additional indications would indicate. More than half imatinib's sales are for off-label use. Some say that due to mutation, three or four non-cross-resistant drugs will be needed to control CML. With OMA and the TKIs, doctors effectively will have two.

A further twist may enhance OMA's prospects. It appears OMA attacks leukemic stem cells in mouse models, something imatinib and dasatinib don't do. If this holds true in humans, it could push OMA into a more prominent role in CML treatment.

Using expected pricing, disease prevalence rates and checking the resultant numbers against those from Frost and Sullivan, I have calculated a discounted cash flow valuation for Chemgenex of $5.50 a share.

Furthermore, I expect Chemgenex's share price to approach my valuation in the next 18 months, making it Australia's next billion dollar biotech.

Chemgenex closed down one cent or 1.08 percent to 92 cents.

Both Marc Sinatra and Biotech Daily editor David Langsam own Chemgenex shares.

Marc Sinatra's Bioguides
Email: marc@biotechdaily.com.au