Evaluate Vantage

February 18, 2010

Gilead’s Quad could square generic challenges to HIV franchise

Lisa Urquhart

Gilead Sciences has gone some way to ensuring that its dominance of the HIV market continues after phase II data from its ‘Quad’ pill presented at the Conference on Retroviruses and Opportunistic Infections showed non-inferiority to its second best-selling drug Atripla.

This early win from the Quad (Elvitegravir + GS 9350 + Truvada) pill has taken on significance because the group, which last year made $5.84bn from selling its HIV drugs, is facing patent expiries of up to 90% of its revenues between 2017 and 2021. But generic challenges to the drugs could come earlier given that Teva Pharmaceutical Industries has filed a generic challenge to both Atripla and Truvada, and Mylan and Aurobindo Pharma both have tentative approvals for the two drugs, as well as Viread. With so much to lose a lot is riding on the success of the new drug.

The Quad is a single pill containing already approved Truvada and two new experimental drugs, elvitegravir and a booster drug GS 9350 (cobicistat). Elvitegravir is an integrase inhibitor, which prevents the RNA of HIV from merging with the DNA of human immune cells. Currently the only other inhibitor on the market is Merck & Co's Isentress, which is also taken with Truvada. The booster element of the pill allows the drug to be taken once daily.

Increased efficacy?

This week’s detailed trial results showed that after 24 weeks 90% of patients who took the Quad had viral loads of less than 50 copies/mL of the HIV virus, compared with 83% of patients taking Atripla, a combination of Gilead’s Truvada and Bristol-Myers Squibb’s Sustiva.

Importantly, the drug also showed fewer total adverse events, at 35% a significant improvement on Atripla’s 57%. Like many current HIV drugs, Atripla has CNS side effects that are largely manifested in psychological disturbances such as abnormal dreams and mood disturbances.

Quad did, however, show increases in creatinine levels in patients, but Gilead has rushed to allay any fears over these by providing additional data to demonstrate that the stage these elevations occur are unlikely to lead to kidney damage or reduced function. As to whether this will be enough for an increasingly cautious FDA remains to be seen.

So while the Quad may not have achieved huge efficacy advantages over Atripla at this stage, which was largely expected because of the small size of the trial, its ease of use (once daily dosing), lower side effect profile and rapid onset of action should lead to increased compliance for the phase III trials and as such could result in better efficacy. These advantages could also provide Gilead with a drug to take over the mantle of Atripla and Truvada and maintain its dominance in HIV.

More of the money

The drug also offers significant economic advantages to Gilead as all four components belong to the group. This is something to consider given the growing dominance of Atripla, whose fourth quarter sales surpassed those of Truvada for the first time last year. The drug also saw a 51% surge in sales to $2.38bn in 2009. If Quad can match or better those sales Gilead might consider throwing its marketing weight behind Quad when it is eventually approved at the expense of Atripla to bolster its own bottom line.

Given that Quad is still only in phase II and a lot still has to happen before it reaches approval, current risk adjusted valuations for the drug are low. According to *EvaluatePharma’s NPV Analyzer* the drug is worth $820m to Gilead. But some analysts obviously impressed with the data are optimistically forecasting peak sales of $4bn for the drug.

But if Gilead successfully defends its patents for Truvada and Atripla - and many believe it will because Teva is only gunning for two of the eight patents the drugs have - the Quad, which is due to start phase III trials later this year, could reach the market ahead of generic competition, allowing Gilead to switch patients and Quad to achieve these lofty looking sales targets.

Defending the castle

Developing a new drug has also gained importance because Gilead now faces a major new challenger in the space following the 2009 alliance between Pfizer and GlaxoSmithKline to combine their HIV franchises under the ViiV alliance (*Glaxo and Pfizer to join forces on HIV, April 16, 2009*).

The tie-up between the two groups was not only a recognition of their individually relatively weak positions in the field compared with Gilead, but also a way to gain access to each others expertise, minimize risk and reduce costs by combining their sales forces. With such a big competitor almost certainly wanting to eat its lunch Gilead needs to up its game.

Further game play could come from the separate data it reported for GS 9350 showing that the booster was as effective in phase II trials as Abbott Laboratories' Norvir. Many see GS 9350, which could be combined with a number of other drugs, including Gilead's own Truvada and Johnson & Johnson's TMC278 to create a protease quad, as yet another way of preserving Gilead's place at the top of the HIV tree and further smoothing over the patent risk fears that are increasingly weighing on the company.