Weaker data could mean slim pickings for Arena in the obesity market

Lisa Urquhart

The eagerly awaited top-line phase III results from Arena Pharmaceuticals' 4,008 patient Blossom trial for obesity drug, lorcaserin, arrived today, but once again showed that the twice-daily pill had failed in one of the key measures of FDA approvability for weight loss treatments and had only questionably met a second. This caused shares in the company to fluctuate wildly, in early trading the stock was down by 15% before settling 4% lower by mid-morning at $4.74.

Of the patients enrolled in the treatment arm, 47.5% lost 5% of their body weight compared with 25% for placebo. While this result ticks the box of the FDA's demand that 35% of patients in the active group lose 5% of baseline body weight, it could fail by a whisker the second portion of this test, that this figure should be approximately double the number of people in the placebo group, i.e. 50%. Lorcaserin also failed the second allowable FDA draft guideline for approvability, that the average weight loss between the placebo group and the active arm be at least 5 percentage points apart. The average weight loss in the trial arm was 4.8% compared with 2.8% in the placebo.

A question of definition

While the criteria for approvability is meeting one of these two measures, Arena was today naturally quick to heavily emphasise the 'approximate' part of the FDA's first guideline. As the group has failed in the second criteria eventual approval of lorcaserin could come down to a simple argument about semantics and just how rigidly the FDA interprets its own guidelines.

The results also showed a slight decline in efficacy from the group's other large scale trial Bloom, which showed average weight loss of 5.8%.

Even the per protocol group, where all patients finished the lorcaserin, failed to hoist itself over the double placebo test, with 34.9% of the placebo group losing 5% of their body weight, compared with 63.2% on lorcaserin. But as the FDA usually looks at intent to treat data anyway, even if lorcaserin had shown better efficacy, this measure would not have mattered.

Approvability

Despite such borderline efficacy data, what lorcaserin appears to have on its side is a very good safety profile. There were no signs of depression or suicidal tendencies in the study or equally importantly valvulopathy, heart valve damage, which has derailed many obesity drugs in the past. The most common complaints were upper respiratory infections and headaches, which occurred almost equally across the treatment and placebo arms.

However, Jacob Plieth, healthcare analyst with Edison Investment Research, questioned whether the data would be strong enough to guarantee the drug approval. “In terms of the FDA approving it the safety profile is in their favour, but in terms of efficacy who knows,” he said.

Market share

Even if lorcaserin does scrape approval out of the current crop of anti-obesity drugs in late stage trials, including Vivus's Qnexa and Orexigen Therapeutics' Contrave, it has shown the lowest level of activity. Therefore it could be consigned to have the lowest sales of all three drugs.

Undoubtedly, with two thirds of Americans thought to be either overweight or obese the market is big enough for all three products, but with Vivus's Qnexa showing the most dramatic weight loss so far, it has the most potential to become a blockbuster drug. Orexigen's Contrave is forecast to be the second-biggest seller with some analysts now predicting peak sales of $700m-$600m, while lorcaserin is now firmly trailing with sales forecast of $300m-$400m.

But the sales split of the drugs is heavily dependent on whether big pharma partners will come on board, with the muscle of large primary healthcare sales forces to penetrate the market.
Given the past and high profile failure of anti-obesity products it is unclear as to whether big pharma has completely written off obesity, due to fears of what would be large class actions if the drugs showed the adverse psychological safety profiles that have derailed the likes of Acomplia and taranabant, or the heart valve damage of Fen-Phen.

On a conference call today Jack Lief, Arena chief executive, indicated that his product had some external interest. “We intend to partner and there is a lot of diligence going on and there are meetings scheduled for our partners to come in following this data,” he said.

But given the drug’s lower efficacy compared with its rivals, the group might only find a smaller licensing partner and could also be the one with the least favourable deal terms.

**Two drugs better than one**

One thing that could eventually drive sales is doctors using the drug in combination with phentermine, something that would boost lorcaserin’s power to reduce weight, and give doctors a combination with a good safety profile. The other drugs that are vying to get approval in the space are also combinations, but in both cases consist of two older products.

At the moment Arena's management team appear to be resistant to considering this as a possibility; given that this would involve more long and costly trials and that Arena has approximately $130m on its balance sheet this is not surprising.

However, if lorcaserin, which is due to be filed by December, fails to get approval the group may have to start to think the unthinkable.

© Copyright 2019 Evaluate Ltd.