

20 August 2019

## **SAREPTA – FOLLOW-UP ON FDA’S SHOCKING DECISION**

Sarepta (one of our most significant positions in the Healthcare M&A certificate) is to fall toady sharply following a bizarre and historical decision for all orphan drugs.

Yesterday the FDA sent a CRL (Complete Response Letter) to the company saying it won’t approve the accelerated approval of golodirsen (would be selling under the name of Vyondys 53 ) injection for the treatment of Duchenne muscular dystrophy (DMD) in patients with a confirmed mutation amenable to exon 53 skipping.

The shocking part of the FDA refusal lies in the fact that the agency cites two reasons which are uncorrelated to the ongoing study and from data that was presented from the company. In fact, the FDA outlines the risk of infection linked to intravenous infusion ports (devices placed just under the skin to give doctors access to a vein) and renal toxicity seen in pre-clinical (animals) models of golodirsen at doses that were ten-fold higher than doses used in clinical studies and observed following administration of other antisense oligonucleotides. The FDA states that renal toxicity was not observed in Study 4053-101, on which the application for golodirsen was based.

Both of the risks outlined by the FDA are without merit in our opinion as the intravenous infusion ports is not a drug-risk per itself and could be overcome very quickly while the risk of overdosing is real for any drug in the market and would take just about every medicine off the market for safety concerns. What makes the difference between an effective drug and a poison is simply the amount of dosing. We are quite shocked to see that the FDA bring a pre-clinical study on the table as those studies are given to the FDA at the beginning of the filing process and the FDA should have come back to the company long-time ago if they had an issue with the pre-clinical data.

We believe the reasons might be different from the ones officially stated by the FDA.

It seems that from talks between the management and Credit Suisse the FDA had reached alignment with FDA on post-marketing commitments, had come to an agreement on the potential label, and FDA had even reviewed the potential Vyondys 53 approval presser. So what did happen in the last few days that made the FDA make a complete U-turn?

We believe that the reasons might be found on the one drug which is already approved (Exondys 51) by the FDA since 2016 and are more related to politics than not with a reliable scientific explanation.

Sarepta got a fast-track approval back in 2016 for Exondys 51 that marked the history of FDA. In fact, despite the AdCom (independent quite rare) voting against the approval of Exondys 51, the FDA overruled (very rare) the AdCom and approved the drug. The decision to approve Exondys 51 was taken by the head (not working at the FDA anymore) of the drug review division, Mrs. Janet Woodcock which clashed with other FDA officials and pushed hard for the approval of this drug on the strength of a surrogate biomarker endpoint even if evidence of any data showing clinical benefits to patients was lacking.

We remind investors that the FDA might approve an orphan drug also if it fails to demonstrate clinical benefit but that the company must come up at a later stage with studies confirming the clinical benefits of the said drug.

As of today, or precisely 3 years later, Sarepta did not come up with a study demonstrating the efficacy of Exondys 51 and showing to the FDA that its drug could improve muscle function in patients, and it might explain yesterday's decision.

As Sarepta is now obliged to discuss with the FDA concerning golodirsen we believe the agency might push the company to present data on Exondys 51, which might represent a short-term risk if the company is unable to do so in a short time frame.

[As already stated in our 12 August 2019 investors' note](#) we believe that Sarepta has a lead over the competition in DMD and most notably Pfizer, but politics and big money might bring the company to a less visible road in the weeks and months to come. We are currently reviewing our positions, and we are to keep our investors updated on the investment decisions we are to take going forward.

While we tend to believe that the FDA decision is more politically driven and company-specific than not scientific-driven it might set a precedent for all the orphan drugs currently in development which is not at all positive and would block developments in this particular field.