

Sarepta Therapeutics: A Gift Before Christmas!

After its rejection in August, the FDA finally approved Sarepta's Duchenne Muscular Dystrophy therapy, Vyondys 53. When the FDA took a negative stance on the drug, we trimmed some of the positions, to lower the risk in Biotech and Healthcare M&A portfolios but maintained a significant weighting in the stock despite the setback.

[After the FDA's surprising and shocking decision this summer](#), the company decided to file an appeal and resubmit its application.

At that time, we wrote that the reasons for rejecting the drug were not fair. The renal toxicity outlined by the agency was based on preclinical studies (in animal models) with a dose ten times higher than that used in the clinical studies. In the 4053-101 study, on which the application was based, no renal toxicity was observed. The risk of overdosing is real for all drugs in the market. The FDA also mentioned that intravenous infusion ports inserted through the skin represented a risk of infection. We also wrote by saying that the intravenous infusion was not drug-related and could have been easily fixed.

Sarepta and the FDA have had a complicated relationship since Exondys 51, which also targets DMD (covering 13% of patients), which received controversial approval in 2016. Exondys-51 sparked a shaky internal debate within FDA officials and was pushed to approval without an Adcom (a panel of independent experts) by the head of the drug review division, Ms. Janet Woodcock.

In August, we also wrote that the unfavorable FDA decision was motivated by political and company-specific considerations rather than drug-specific considerations.

The agency finally understood that DMD is a rare and 100% fatal disease.

The Duchenne disease is caused by a genetic mutation that prevents the body from producing dystrophin, a protein that muscles need to function correctly. Without this essential protein, muscle tissues are damaged and weakened. It mainly affects males and occurs in 1 in 3'500 to 5'000 males born worldwide. The average lifespan is mid-to-late 20s and diagnosed between ages 4 and 5.

Vyondys 53 is targeting 8% of patients who respond to exon 53 skipplings. Patients with an exon 53 genetic mutation are not able to produce enough dystrophin. The drug is an antisense RNA therapy that binds to exon 53 of pre-mRNA dystrophin, resulting in the exclusion of said exon. The clinical data, used to support the approval, showed that dystrophin levels increased from 0.1% to 1.02% (normal level) after 48 weeks.

The company has still to prove the clinical benefits based on real-world data. All drugs approved under an orphan drug designation (priority review program within the FDA) need to come up with follow-on data. Data from patients currently enrolled are not to be expected anytime before 2024.

The price of Vyondys 53 will be on par with Exondys 51, at \$300'000 a year per 20kg. Along with its first approved drug, Exondys 51, Sarepta will offer a treatment option for approximately 20% of the patients having DMD in the U.S.

The FDA is definitely on fire to give accelerated approvals before 2020. This approval also confirms our thesis on rare diseases. We believe that rare diseases are among the best targets for the next generation of drugs, and this is only the beginning of the wave of approvals expected in the coming years. As mentioned in our latest [investment recipes published on the 4th of December](#), orphan drugs are very attractive to biotechnology companies and provide a multi-billion revenue opportunity. We also believe that RNA-based treatments are, in our opinion, one of the best strategies for treating rare diseases.

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