2024 Superconvergence BioRevolution Series: A Blockbuster Gene Therapy?

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Key Takeaways

- The biotechnology sector has not seen a sustained rally in 2024 despite initial optimism and ongoing progress.
- Sarepta Therapeutics' Elevidys, a $3.2 million gene therapy for Duchenne muscular dystrophy, received expanded FDA approval in June 2024, with positive indications on insurance coverage being a key factor.
- Biotechnology investments are high risk, and diversification through funds like the WisdomTree BioRevolution Fund (WDNA) can help mitigate these risks.

At WisdomTree, we work with Dr. Jamie Metzl on a strategy that we term the BioRevolution. We believe that we are on the precipice of a remarkable period that could last a few decades where we challenge and ultimately evolve how we do such things as:

- Handle human health care.
- Consider growing food for an expanding global population.
- Generate novel materials, chemicals and energy from biological sources.
- Think about storing massive amounts of data with higher density and fidelity than we have in the past.

Dr. Metzl recently published the book, *Superconvergence: How the Genetics, Biotech, and AI Revolutions Will Transform our Lives, Work, and World.* We aim to publish a series of blog posts that draw attention to some of the ideas presented in the book.

The bottom line: Thematic investing, in a sense, is about storytelling. *Superconvergence* does a great job of conveying the narrative behind the WisdomTree BioRevolution Index, which is tracked, after fees and expenses, by the WisdomTree BioRevolution Fund (WDNA).

Preparing for a Blockbuster Gene Therapy

As we started 2024, we were very excited about the prospects in the biotechnology area of the equity markets. Our thinking was simple—this is an area with the potential to impact so many lives and one

where we, as a global society, want to see advances. Our view was that, after years of relatively lackluster investment performance, the space was due for a rebound.

For the better part of the first eight months of 2024, our view has not proven correct. Biotechnology equities have performed in fits and starts, but we have not seen any sort of sustained rally in the space. In the beginning of 2024, it was true that the market was tending to look at the policy of the U.S. Federal Reserve, hoping for policy rate cuts, and as we write these words roughly halfway through August 2024, the market is looking at this very same thing.

However, the companies are continuing to make progress.

The Case of Sarepta Therapeutics: A $3 Million Drug

Given the hurdles that biotechnology companies need to clear in order to develop and then produce successful therapies, it's amazing that we have these medicines. There are so many risks, and many don't fit into company fundamentals or financial statements.

Sarepta Therapeutics has focused on Duchenne muscular dystrophy (DMD). This is a rare, debilitating disease that impacts a few hundred thousand people worldwide. It is caused by a mutation on one of a mother's X-chromosomes, and leads to difficulties in the body producing dystrophin, which protects muscles from degrading in the presence of enzymes.1

Sarepta developed Elevidys, a gene therapy that, simply put, inserts a gene that seeks to alleviate the issue in the production of dystrophin. It's a great example of a genetic cause being determined and researchers being able to get to a point where they can, essentially, fix the problem.

The cost of this therapy is $3.2 million. The Food and Drug Administration (FDA) expanded the initial approval of this therapy in an announcement on June 20, 2024. Importantly, approval and expanded use did not come because people receive this and are cured. As this is a severe and rare disease, and since there are no other options, the FDA wants to ensure the treatment option is on the table.1

Given a medical therapy with a multi-million dollar price tag, in the U.S. market, many would be wondering whether it is covered by insurance. There are indications that some of the large insurers and Medicaid have written policies on the label and that, if it is prescribed, they won't fight against allowing the therapy by resisting payment.1

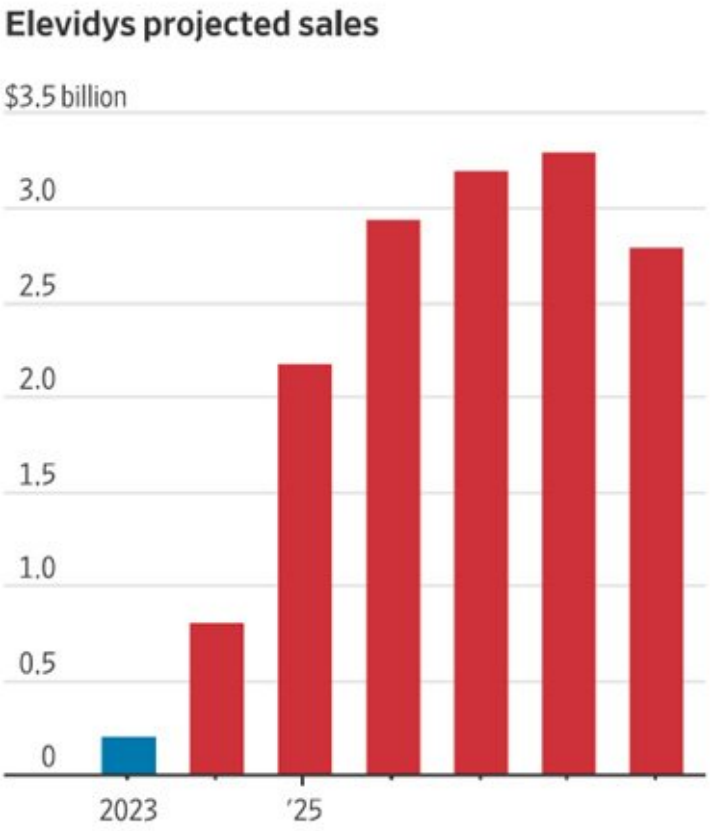
Translating Projections into Realities

As we look at companies in the biotechnology space, it becomes clear that there are so many ways to fail. There is no guarantee a therapy can be developed. There is no guarantee that such a therapy can move through all of the trial phases and secure FDA approval. Then, one has to consider whether insurance providers will pay for the therapy. While all of this is happening, maybe a another company will find a different, more effective approach, taking away the potential market. Maybe negative side effects will be uncovered along the way.

Every therapy requires talented people working extremely hard with massive investments of time and money over many years. Most will never achieve revenues of billions of dollars—blockbuster status.

Elevidys, as we write in August 2024, is a long way from blockbuster status. However, if things go according to analyst projections (shown in figure 1), the therapy could lead to a few billion in revenue in only a couple of years. The number of people in the U.S. with DMD is a known quantity, as well as the typical number of new cases over a given year. As designed, this is currently a one-time therapy. It is therefore reasonable to consider different sorts of potential revenue estimates.

Figure 1: Elevidys Projected Sales (Full years, up to 2029)



Source: David Wainer, "A $3 Million Gene-Therapy Maker at a Bargain Price," *Wall Street Journal*, 8/19/24. **Forecasts are not an indicator of future performance.**

It's possible that, with so many risks on the horizon with any individual biotechnology stock, it makes sense to consider the so-called biggest risk at any single time. In 2024, Sarepta investors were focused on securing the expanded approval from the FDA. This approval was secured, and the share price reacted, positively, roughly 30% on the news. Since then—and of course from June 20, 2024, until the second half of August there has been market volatility—shares have given up a portion of these gains.1

The WisdomTree BioRevolution Fund (WDNA)

Think of all the ways in which an analyst would have to evaluate Sarepta Pharmaceuticals in recent years:

- There is the overall science of DMD and the probability that a therapy can be developed.
- There is then the probability that the therapy delivers well enough through the various phases of the FDA's clinical approval process to be approved.2
- There was the recent discussion of expanded approval, which occurred about one year after the initial approval.3
- While all of this is happening, the usual financial analysis of revenues, expenses, cash flows—that is all still there.
- There is also the progress in different markets beyond the U.S. that needs to be considered because it can dramatically impact the size of the addressable market.

Investors have the option to look at any single company, of course, but one of the reasons we developed the WisdomTree BioRevolution Fund (WDNA) was to recognize that diversification could be of particular importance in this very high-risk space. As of August 16, 2024, there were 91 individual equity holdings. Sarepta was one of these, weighted at roughly 1.6%.4

One company at a 1.6% weight is not going to drive a portfolio of more than 90 equities toward any particular result, but we note that the story of Sarepta and Elevidys is an important illustration of where we believe we are in the biotechnology space. We believe that the convergence of what we are seeing in areas like artificial intelligence and cloud computing is contributing to us being able to pursue more paths of interesting research, faster, and that we will keep hearing about more and more potential gene therapies. For those investors with the appropriate degree of patience, the coming years could get very interesting.

1 Source: David Wainer, "A $3 Million Gene-Therapy Maker at a Bargain Price," *Wall Street Journal*, 8/19/24.

2 Source: "FDA Approves First Gene Therapy for Treatment of Certain Patients with Duchenne Muscular Dystrophy," *FDA Press Release*, 6/22/23.

3 Source: "FDA Expands Approval of Gene Therapy for Patients with Duchenne Muscular Dystrophy," *FDA Press Release*, 6/20/24.

4 Source: "Wisdomtree Biorevolution Fund." *WisdomTree*, www.wisdomtree.com/investments/etfs/mega-trends/wdna.

Important Risks Related to this Article

For current holdings of WDNA, please click here. Holdings are subject to risk and change.

There are risks associated with investing, including the possible loss of principal. The Fund invests in BioRevolution companies, which are companies significantly transformed by advancements in genetics and biotechnology. BioRevolution companies face intense competition and potentially rapid product obsolescence. These companies may be adversely affected by the loss or impairment of intellectual property rights and other proprietary information or changes in government regulations or policies. Additionally, BioRevolution companies may be subject to risks associated with genetic analysis. The Fund invests in the securities included in, or representative of, its Index regardless of their investment merit and the Fund does not attempt to outperform its Index or take defensive positions in declining markets. The composition of the Index is governed by an Index Committee and the Index may not perform as intended. Please read the Fund's prospectus for specific details regarding the Fund's risk profile.