2024 SUPERCONVERGENCE BIOREVOLUTION SERIES: JOURNEY TO THE MRNA VACCINE & BEYOND

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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).

A Vaccine Revolution

Many people may not realize that to synthesize the influenza vaccine, we depend largely on using eggs somewhat as mini manufacturing units. The concept is to create weakened influenza virus particles such that the human immune system can be better prepared to respond strongly to the real thing during flu season.[1]

However, this is not the only way to synthesize vaccines. From *Superconvergence*[2]*:*

> *While it seemed to many people that the COVID-19 mRNA vaccines sprang out of nowhere, they actually resulted from at least 150 years of work, starting from the discovery of nucleic acids in the 1860s to messenger RNAs a century later, along with 60 years of work and a steady stream of contributions from thousands of people and hundreds of labs and companies across multiple continents. These advances had made it possible to synthesize mRNAs, genetically alter them so they aren't prematurely destroyed by our immune cells, and wrap them in microscopic, electrically charged balls of fat called lipid nanoparticles to keep them intact long enough to do our bidding. For a decade prior to the COVID-19 outbreak, scientists at the US National Institutes of Health (NIH) had been working aggressively to develop a faster vaccine development process, with a particular focus on using AI analytics to identify specific targets for how best to counter various viruses.*

Where things get more interesting is when we see how different technologies that have each been undergoing decades of development converge—and the mRNA vaccine story, which

is ongoing, is an excellent example in this regard. Basically:

- Through the work done on the Human Genome Project, we learned how to better sequence DNA data in different ways from different organisms. This was an important foundation.
- At the same time, we can recognize that DNA and RNA represent different sequences of chemical instructions—information—at their core. Processing power has been steadily increasing through such principles as Moore's Law, and we have also seen speed ups in data transmission and increasing ease of data storage.
- Cloud computing infrastructure has been built, such that those with the appropriate resources and need can instantly spool up powerful computing platforms, on-demand, to accomplish specific tasks.
- AI algorithms and machine learning capabilities can allow for the recognition of patterns in almost any kind of data.

This allowed for the following, from *Superconvergence:*

> *Within two days of receiving the computer file of the sequenced genome, they had come up with the recipe for what became the Moderna vaccine, which incorporated the innovations of decades of research and the work of multiple scientists, particularly from the NIH and the Universities of Texas and Pennsylvania. Not a single wet-lab experiment was involved.*
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> *Two months later, the first human trial began. Nine months after that, the first vaccine dose was administered under an emergency use approval by the US Food and Drug Administration (FDA). As of 2024, around 12 billion COVID-19 vaccine doses had been administered to people across the globe, a large percentage of those using mRNA vaccines.*
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> *By the time later variants of the SARS-CoV-2 virus, like the infamous Omicron, caused COVID-19 infections to spike worldwide in late 2021 and early 2022, developing variant-specific boosters had become even faster. The mRNA vaccines had increasingly become "plug and play." Companies like Moderna and Pfizer/BioNTech rapidly developed single-dose mRNA vaccine boosters that targeted the early Omicron variant known as BA1, which performed well in human clinical trials.*

The bottom line is that the foundation was there, and multiple technologies were ready to respond as scientists and researchers sought to have as fast a solution as possible to help the world re-open following the Covid-19 pandemic.

mRNA's Story Doesn't End with Covid-19

Moderna was the company-embodiment of the mRNA story. Its Covid jab generated more than $40 billion in revenue. The company at one point had a market capitalization of $160 billion.[3]

However, Moderna has an issue—how can it convince market participants that mRNA is a far broader platform for fighting different diseases than simply being a solution for Covid-19?

In *Superconvergence,* Metzl noted some of the possibilities:

> *The mRNA vaccines weren't just a new approach to vaccination but a new platform for delivering alternate sets of instructions to our bodies. Active trials are now underway using similar mRNA delivery platforms to treat cancer, HIV, malaria, tuberculosis, Alzheimer's, herpes, respiratory syncytial virus (RSV), inherited metabolic disorders, cystic fibrosis, multiple sclerosis, heart disease, and asthma.*

The human immune system is a fascinating set of different capabilities. It is essentially imbued with a capacity to recognize foreign cells and develop a response that, in most cases, in most people, repels what could otherwise be a severe infection.

What If You Could Instruct this System to Do Different Things On-Demand?

There is a use case where patients have experienced a treatment for melanoma. Doctors are able to get the requisite sample from cancer cells that can then be used, through a set of mRNA instructions, to train a person's individual immune system to attack that person's specific cancer cells. These cells have certain characteristics, just like the so-called spike-protein in the Covid-19 virus.[4]

The notable element is if the immune system can attack ONLY cancerous cells, that is a stepwise improvement over chemotherapy, which is something that affects many different cells. While it is not yet widespread, there are signs that this type of therapy could have a very promising future.

[1] Source: https://www.cdc.gov/flu/prevent/cell-based.htm#:~:text=Most%20inactivated%20flu%20vaccines%20are,instead%20of%20in%20hen's%20eggs.

[2] Jamie Metzl, *Superconvergence: How the Genetics, Biotech, and AI Revolutions Will Transform our Lives, Work, and World*, 2024.

[3] Source: Oliver Barnes, "Moderna Wins Second Approval with Vaccine Targeting RSV Infection," *Financial Times*, 5/31/24.

[4] Source: Elie Dolgin, "How Customized RNA Vaccines Might Halt Cancer," *Nature*, 6/13/24.

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