HOW TO 10X YOUR MONEY

IN AMERICA'S LAST DIGITAL LEAP

BROWNSTONE RESEARCH

How to 10X Your Money in America's Last Digital Leap

By Jeff Brown, Editor, *Exponential Tech Investor*

Last July, as I was flipping through some recent research publications, one particular paper caught my attention.

A joint team of researchers from Duke and the National University of Singapore published a remarkable look at the immune system and how effectively our bodies can build T cell immunity to coronaviruses.

T cells (and B cells) are the types of white blood cells that are critical to what is referred to as our adaptive immune system. Our adaptive immune system fights invading pathogens and other foreign molecules using these T cells and B cells.

T cell receptors (TCRs) exist on the surface of our T cells, and they are "programmed" to recognize antigens, which are proteins that are produced as a result of exposure to a virus or pathogen. That way, if we have been exposed to a pathogen, our bodies learn to recognize and fight off the disease in the future.

Needless to say, the timing of the research was highly relevant considering that it was only in March of last year when the world came to terms with the fact that COVID-19 (SARS-CoV-2) had spread far and wide. This research should have been disseminated widely, but it wasn't. Sadly, it was largely ignored.

The research demonstrated that patients who were exposed to SARS-CoV-1 during the SARS outbreak in the early 2000s and recovered still had T cell memory that reacted to exposure to the same coronavirus over 17 years later. That's right – almost two decades of natural immunity and counting.

Ironically, while I wasn't part of the research, I was actually one of those people exposed to the virus. I was on a business trip in Hong Kong at the absolute height of the SARS-CoV-1 outbreak in 2003. I must have contracted the virus on that trip, but I never knew it. I was asymptomatic, as most people were.

It wasn't until I was tested a few months after I caught COVID-19 last March that I realized I had been exposed to both.

Interestingly, the research also demonstrated that patients who had already been exposed to SARS-CoV-1 demonstrated strong cross-reactivity when exposed to COVID-19. Put more simply, those patients' T cell immunity, developed back in 2003 from SARS-CoV-1, protected them against COVID-19.

Also surprising was that the research demonstrated that preexisting T cell memory "learned" from exposure to common cold coronaviruses could cross-recognize COVID-19 down to the exact molecular structure. That's right – exposure to common cold coronaviruses actually helps train our immune system to fight off COVID-19.

And that's why the majority of cases of COVID-19 go undetected. They are asymptomatic. And this is also why many cases that do present symptoms are mild and don't even require a visit to a doctor.

The Crisis That Fueled Breakthroughs

What a different year 2020 would have been if the media and politicians had read and understood this research. The fear and panic could have been completely avoided. But sadly, the political narratives won at great devastation and cost that we are only now beginning to understand.

But something good has come out of all of this. Not only have we seen incredible advancements in messenger RNA (mRNA) technology used to develop vaccines, the COVID-19 pandemic has created a lot of awareness and excitement around our immune systems.

Coincidentally, almost exactly a year prior to the research being published, something highly relevant happened. A small biotechnology company focused on our adaptive immune systems and backed by Celgene, Illumina, LabCorp, Microsoft, and a small group of biotech venture capitalists went public.

Shares flew out of the gate, opening up 141%. But normal investors never had a chance. Only the insiders had the chance to take profits off the table in the weeks that followed.

Regular readers know that I don't like to recommend stocks during this window for traditional IPOs. There is too much market manipulation during the first 180 days of trading. I also like to watch companies go through a couple cycles of earnings announcements to build confidence in the management team and the company's progress.

But that time has finally passed for this exciting biotech company that went public in June 2019.

In this report, we're going to invest in **Adaptive Biotechnologies (ADPT)** as it uses our immune systems to diagnose and treat disease.

Welcome to *Exponential Tech Investor*

Welcome to *Exponential Tech Investor*. I'm Jeff Brown, your editor.

For nearly 30 years, I worked as a technology executive for firms like Qualcomm, NXP Semiconductors, and Juniper Networks. I've earned degrees from Purdue University and the London Business School. I've also received professional certificates from MIT, Stanford, and most recently the University of California, Berkeley, School of Law. And I am also an alumnus of Yale University's School of Management.

I'm also an active angel investor in early stage technology companies. I've invested in dozens of private deals over the years. I don't tell you all this to brag. But with so many so-called technology experts out there, it's important that readers know that I'm truly committed to the world of bleeding-edge technology.

Here in *Exponential Tech Investor*, we invest in companies on the bleeding edge of technological progress. I'm talking about companies that are reshaping and sometimes creating entire industries.

These are the major players making incredible progress in 5G wireless networks, artificial intelligence, decentralized manufacturing, cloud computing, and – as this report's company shows – biotechnology.

This is one of the trends I am most excited about. As I wrote above, the COVID-19 pandemic has thrown a spotlight on this space… and with this recommendation, we're perfectly positioned to profit.

Our Incredible Immune System

Adaptive Biotechnologies is, of course, named

after our adaptive immune system. This exciting biotech company is focused on immune medicine and using the immune system for diagnosing and treating disease.

ADPT was originally focused on immunosequencing. We can think of this like sequencing every T cell receptor in our immune system in order to understand and quantify the health and status of our immune system. This kind of sequencing can be done with incredible sensitivity and specificity down to identifying a single cell out of a million cells.

It's no surprise that Illumina, the giant in genetic sequencing, found this company an exciting early stage investment.

Put another way, Adaptive sequences the genetics of the human immune system in order to understand exactly how the immune system detects and recovers from a disease. Since its founding in 2009, Adaptive has sequenced and characterized more than 58 billion immune receptors.

Adaptive Bio's "One" Immune Medicine Platform

Source: Adaptive Biotechnologies

Adaptive has been the pioneer in this space with its immunoSEQ product that is used by more than 165 biopharma companies around the world. Naturally, this product has been the core of Adaptive's business for years.

Combined with its immunoSEQ T-MAP product, which maps T cell immune responses to specific antigens, this sequencing business historically made up the majority of Adaptive's revenues.

But it's been quickly expanding its capabilities...

"Full Stack" Biotech

To characterize Adaptive as just the world's best immunosequencing company would be a mistake. To use a software analogy, I like to think of Adaptive as a "full stack" biotechnology company.

In software, "full stack" refers to the entire architecture of a software application. It includes how and where an application is hosted, how it connects with databases, how it functions with other applications, and, of course, how users interact with the software.

And Adaptive has a similarly broad scope for its own products and services.

It doesn't just build technology that enables sequencing, immune research, and mapping of the immune system. Adaptive also built a diagnostics business capable of detecting and monitoring minimal residual disease (MRD). It also developed products that can detect past infections or diseases. Thus, it can detect whether someone has natural cellular immunity or not.

And the final part of the "stack" is using all of this incredible data about the immune system that Adaptive has built over the last decade for the purpose of drug discovery.

Research, mapping, characterization, diagnostics, detection, drug discovery, and ultimately drug development… all in one company. This is a big play. Adaptive is swinging for the fences.

And Adaptive's work on COVID-19 gives us a perfect example of this in action…

Purpose-Built Detection

The University of Oxford and AstraZeneca used Adaptive's technology to map the immune system interaction with specific COVID-19 antigens. The AstraZeneca vaccine was ultimately authorized for emergency use in the U.K. in December 2020 and for further use by the World Health Organization (WHO) this February.

Adaptive took this "full stack" work of sequencing, mapping, and characterizing the immune system with regards to COVID-19 antigens, and it developed T-Detect.

This diagnostics product detects prior infection of COVID-19 using a single blood draw, and it has incredible accuracy of 97.1%. And T-Detect was approved by the Food and Drug Administration (FDA) in March for emergency use.

I ordered the T-Detect kit right away and received one at my house a couple of days later. Whenever I can, I always like to test the products and services of the companies that I research, as the first-hand experience always leads to better insights.

This test is the very first of its kind. And while this one specifically tests for prior infection of COVID-19, the reality is that this new product is just the beginning.

This is a breakthrough in the world of diagnostics. The COVID-19 test is just the first.

In fact, prior to the pandemic, Adaptive was already working aggressively on cellular diagnostics tests for Lyme disease, Celiac disease, and Crohn's disease. And a program for the early detection of ovarian cancer is also in its pipeline.

And for all these diseases, Adaptive is focused on one end goal…

One Blood Draw, Many Results

The goal, which Adaptive will achieve, is to have one single blood draw result in a spectrum of disease results. I went through a health check-up recently where I had about 15 vials of blood drawn to test for a variety of conditions.

We can imagine how just one blood draw and one diagnostics test would dramatically reduce costs and quickly identify diseases to improve overall health outcomes.

Adaptive's technology will also enable population immunomics. This enables us to study the human immune system response to a virus or pathogen at a population level.

That's right… If we choose to use T-Detect at a population level, we can accurately understand what percentage of the population has already had COVID-19 and built natural immunity. If we do so, I'm willing to bet that the numbers are much higher than we might think.

More importantly, natural immunity is stronger and longer lasting than immunity from any vaccine. And understanding its prevalence will inform us as to whether or not we have reached herd immunity.

If there is one thing that we have been missing throughout this entire pandemic, it has been accurate data. T-Detect is far more accurate than any serology test for antibodies. And it can detect the past presence of COVID-19 no matter when

we were infected. I can only hope that this test is used widely, and the population-level results are published for everyone's benefit.

Before we go further, I want to emphasize one key point. Adaptive Bio is not a play on COVID-19.

That may come as a surprise. Yes, Adaptive will grow and profit from the sales of T-Detect. And it will potentially benefit from the development of an antibody therapy for COVID-19. But that's not the big picture. It's not the "full stack."

When I look at Adaptive, I see a company that leveraged its platform (its "full stack") to deliver an extremely valuable product (T-Detect) to market that addresses a critical need during the pandemic.

But our investment thesis for this company is much larger...

A Smart Capital Raise

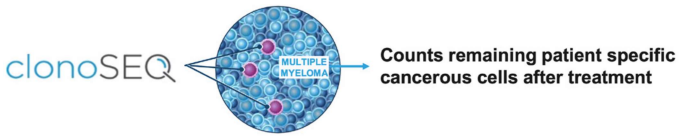
Adaptive was smart. Last year, COVID-19 heightened the excitement and focus on developing diagnostics and therapies.

So Adaptive quickly capitalized on the situation. It announced a secondary offering last July to take advantage of the 144% run-up in its share price since its initial public offering (IPO) the year prior. On the back of excitement about T-Detect and the potential of its powerful antibody therapy for COVID-19, it raised an additional $368 million on July 15, 2020.

This was a great move, as the company more than doubled what it raised from its 2019 IPO. Adaptive now sits on more than $800 million in cash. That's enough to fund research and development (R&D) for the next three years or until it starts generating free cash flow.

And one of its key areas of R&D has been detecting and monitoring minimal residual disease (MRD). MRD refers to small numbers of cancerous cells that remain in a person either during or following treatment when the patient is in remission. It's a major cause of relapse.

Adaptive's clonoSEQ is the first test authorized by the FDA for the detection and monitoring of patients with multiple myeloma (MM), B cell acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL).



Source: Adaptive Biotechnologies

The specificity of these tests is incredible. ClonoSEQ can find one cancerous cell among a million cells. For patients who have undergone therapy for cancer, clonoSEQ gives a very precise understanding of how successful the treatment has been.

Adaptive has done a great job getting its diagnostic test for these cancers approved for reimbursement through insurance. As a result, about 225 million people are now covered. ClonoSEQ is used in literally every single one of the National Comprehensive Cancer Network (NCCN) centers around the U.S.

More than 40 biopharma companies are now using clonoSEQ in over 190 clinical trials. Needless to say, it has become the industry standard for diagnostic testing in blood cancers.

At the moment, clonoSEQ is approved for ALL and MM in bone marrow and CLL in blood. And over the course of the next 24 months, it should receive approval for ALL and MM in blood and expand its support for non-Hodgkin's lymphoma (NHL).

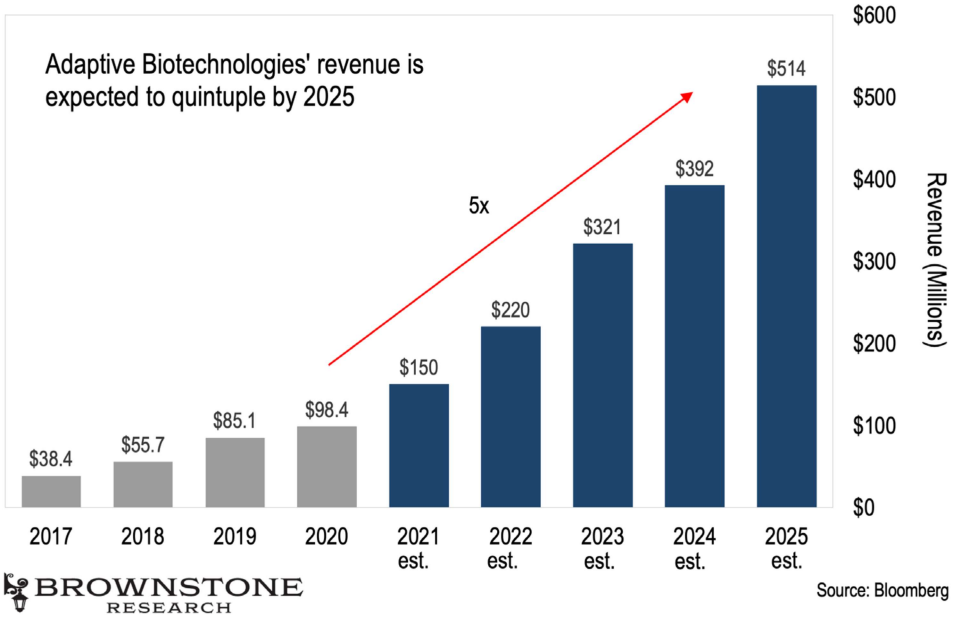
In total, by 2024 we can expect that Adaptive's

clonoSEQ product will be accessible to about 4.6 million cancer patients around the world.

We can view Adaptive as a company with two business lines that are growing exponentially at fantastic gross margins:

- Life Science Research – immunoSEQ products (sequencing and mapping)
- Clinical Diagnostics – clonoSEQ and T-Detect (detection of disease or past infection)

Adaptive Biotechnologies Annual Revenue



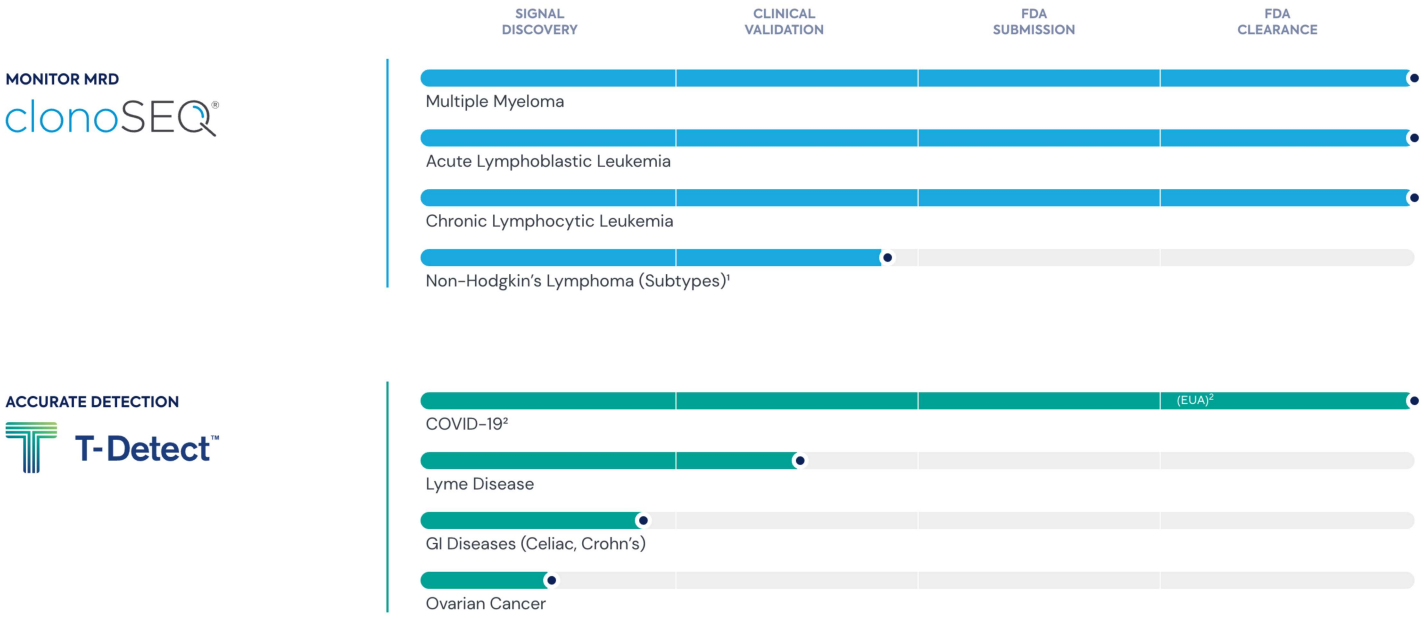
These business lines are a key part of Adaptive Biosciences' growth potential, but that's still not the whole picture...

The End Game

Here is the best part. Adaptive will grow its revenue this year from these two business lines at more than 50% year over year with 73% gross margins. And as it does so, it will gain an even larger competitive advantage in understanding the human immune system.

And this fuels the third line of business that has the largest upside – drug discovery.

Adaptive Biotechnologies' Diagnostics Pipeline



Source: Adaptive Biotechnologies

Adaptive's decade-long push into R&D in the immune system culminated in a $2.3 billion deal with biotechnology giant Genentech in 2019. Genentech is a wholly owned division of pharmaceutical powerhouse Roche following its acquisition for nearly $47 billion back in 2009.

Adaptive's partnership with Genentech is to develop TCR-based cell therapies for the purpose of delivering personalized cancer therapies. Adaptive will develop a personalized cell therapy based on patient-specific T cell receptors. This is the definition of personalized and precision medicine.

The value of the deal with Genentech is hard to overstate. It's worth about half of Adaptive's current $5 billion valuation. But the value of Adaptive's own in-house, personalized TCR-based cell therapies is ultimately worth much more.

And that's why I'm so excited about this recommendation...

A Dominant Patent Portfolio

No other company has developed as deep an understanding of the adaptive immune system as Adaptive Bio.

The company already has 386 issued patents across its "full stack" immune medicine platform and 65 more pending patent applications. Adaptive has a stated goal of ultimately generating a return on its patent portfolio.

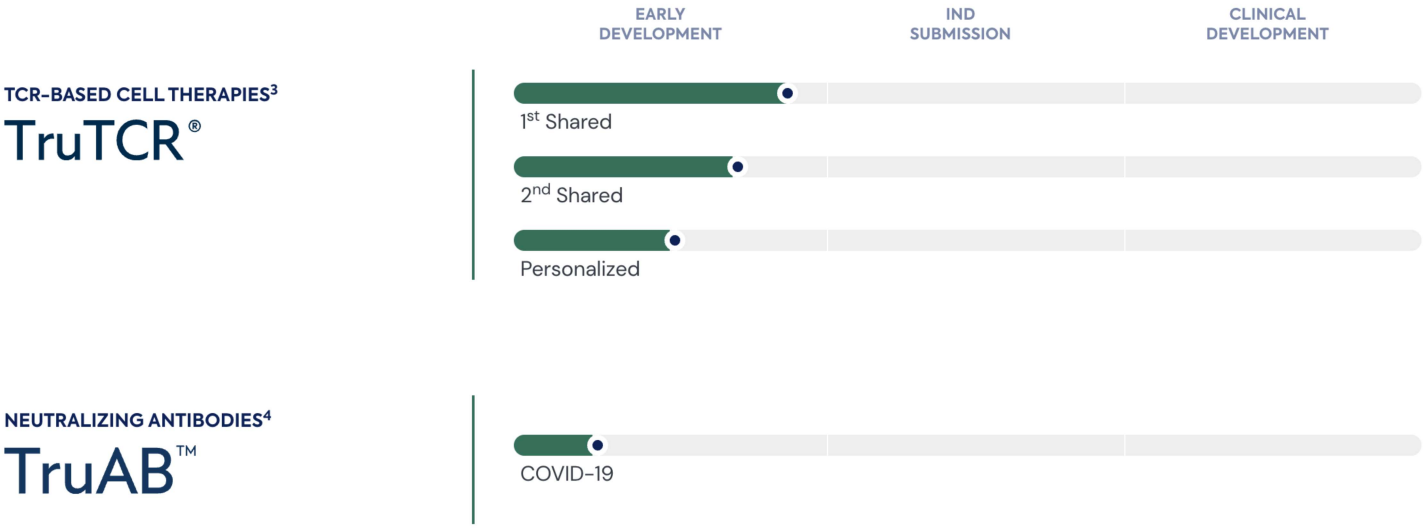
Of course, most companies will say that they want to do this, but Adaptive reminds me a lot of another portfolio company – Editas Medicine (EDIT). Its adaptive immune system patent portfolio is as valuable in this space as Editas' patent portfolio is to CRISPR genetic editing technology.

And a key part of Adaptive's story is its secret weapon for building its map of 58 billion immune receptors – artificial intelligence (AI).

Back in December of 2017, Adaptive struck a deal with Microsoft to collaborate on mapping out the relationships of these T cell receptors with antigens.

The fact that it involved Microsoft wasn't what made it a smart deal. What I liked was the deal structure.

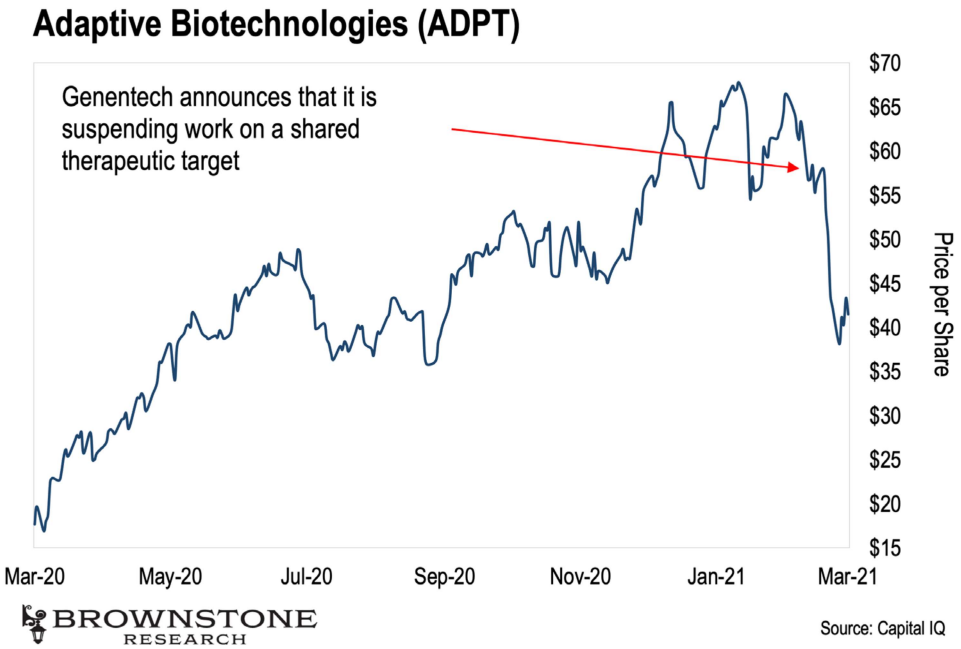
Adaptive Biotechnologies' Drug Discovery Pipeline



Source: Adaptive Biotechnologies

The "collaboration" was actually a $45 million investment by Microsoft into Adaptive Bio. In exchange, Adaptive would receive access to Microsoft's machine learning technology and would agree to spend $12 million over the seven-year term of the agreement on Microsoft Azure cloud services.

Microsoft is known for making these kinds of deals. I refer to them as "buying business." If that's how Microsoft has to win, I'm not impressed.



But for a company like Adaptive Bio, this was a smart deal. It received $45 million and only needs to spend $12 million of that on cloud services – which it needs to buy anyway.

Adaptive Bio is attempting to do for the immune system what genetic editing companies are doing for mutations in the human genome. By using artificial intelligence (machine learning), it is accelerating the process for both diagnostic purposes and drug discovery.

This is one of the single biggest stories of this decade.

Opportunistic Timing

So why invest in Adaptive Biotechnologies?

Well, an overreaction has provided us the perfect window to establish a position.

Remember that strategic $2.3 billion collaboration deal with Genentech? On March 2, Genentech announced that it had suspended the research on its first cancer target due to safety issues.

There weren't many details shared at all, and it was entirely Genentech's decision. This first target was still in pre-clinical stages. Therefore, it wasn't under review by the FDA.

In pre-clinical stages, these kinds of decisions are normal. Genentech has a list of potential candidates. Since it is the one paying, it is going to choose the targets that have the highest probability of success. The fact that it decided to pass on its first target is simply no big deal.

The key point is that there was no change at all to the collaboration between Adaptive and Genentech. They're going full steam ahead.

And from a financial perspective, only about $4–5 million of revenue will slip from 2021 into 2022. The market was disappointed because it was expecting an investigational new drug (IND) application this quarter, but now we can expect that to happen in early 2022.

This resulted in a Goldman Sachs downgrade for 2021… and thus a fantastic opportunity for us to step in at a good price and invest ahead of future growth catalysts.

This is one of the most important ways that we can stack the deck in our favor rather than being taken advantage of by Wall Street. When they make silly, short-term decisions, we pounce on great companies and hold for fantastic long-term capital gains.

When I look at a company like Adaptive, it reminds me of where messenger RNA (mRNA) companies were back in 2019.

Moderna is a perfect example. It was roughly a $5 billion company back in 2019 with what was perceived to be a very bloated and distracted portfolio of possible drug candidates. But its platform for mRNA was solid, and the company is now worth 10 times what it was back then.

Adaptive has the potential to do for the adaptive immune system over the next couple of years what Moderna was able to do with mRNA.

And while we likely won't have the rare confluence of events that happened around COVID-19 over the next two years (hopefully), Adaptive is already benefiting from renewed interest in the human immune system and the potential for accelerated immunotherapies. This is an investment with 5X return potential over the next few years.

Let's make sure to take advantage of this opportunity.

Action to Take: Please refer to our model portfolio for the most current recommended buy-up-to price for **Adaptive Biotechnologies (ADPT)**. Be sure to use a limit order when placing trades. For the time being, we will hold ADPT with no stop loss. Always remember to use rational position sizing.

Risk Management: We will be holding this position without a stop loss. So let's remember to always keep our position size rational. And remember, I never recommend going "all in" on any one investment.

I'm excited for *Exponential Tech* readers to start building a position in this company.

And even more exciting, we have included a second bonus recommendation for this last digital leap taking place. It's another stock with the potential to transform the entire precision medicine space. Just read on to find out all about this greenfield opportunity...

Bonus Recommendation: Beam Therapeutics (BEAM)

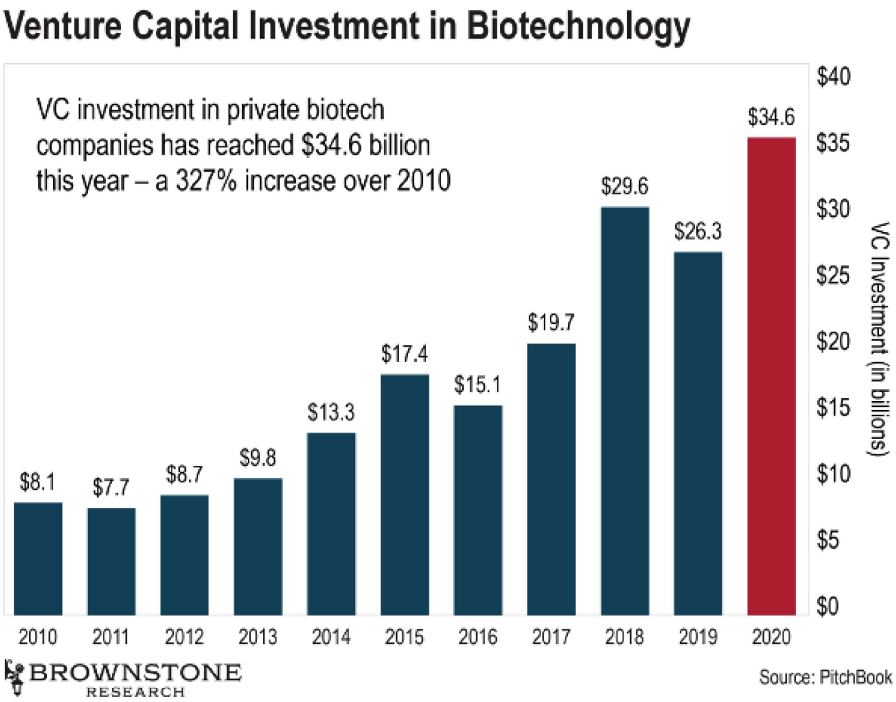
I've been tracking **Beam Therapeutics (BEAM)** since its founding a few years ago for reasons that I'll explain in a bit. Beam first and foremost is a genetic editing company. Some refer to it as the "next generation" of genetic editing. From my perspective, it is the beginning of the next wave of private genetic editing companies to hit the public markets.

I was incredibly excited when Beam went public in early February 2020, paving the way for a record-breaking streak of venture capital (VC) funding for the biotech industry.

And 2020 was a record-breaking year for biotech initial public offerings (IPOs) as well. Biotech IPOs raised over $20 billion.

This is fantastic news for our biotech holdings in our *Exponential Tech Investor* model portfolio. Awareness in this space has never been higher, and slowly but surely, Wall Street is starting to figure out how valuable these companies and their intellectual property really are.

And that brings us to the company in this report.



Beam Therapeutics is built on a new technique for genetic editing called "base editing." Base editing is unique because it precisely edits a single DNA base pair. The technology converts one base to another base by rearranging the atoms of the DNA base. More importantly, it does so without cutting the DNA.

This differs from CRISPR (clustered regularly interspaced short palindromic repeats) technology, which uses a CRISPR-associated protein to create a double-stranded break in the DNA in order to make genetic edits.

Before I go further, I'd like to make one point clear. Beam's approach is not a replacement for the CRISPR technology used by other biotech companies like Editas, Intellia, and CRISPR Therapeutics. We can think of this as a complementary genetic editing platform. For certain genetic conditions, certain enzymes are more effective. The same will be true with a CRISPR-based edit versus a base edit.

We can think of it like this...

A mechanic has several options when fixing a car. He or she may need to simply replace one part. Perhaps the mechanic needs to remove an obstruction. And occasionally, a mechanic may need to remove an entire engine – "breaking" the vehicle apart – in order to fix the problem.

Obviously, that's not a perfect analogy. And I'm not suggesting that curing disease is the same thing as fixing our pickup truck. But it gives us an idea of the different approaches CRISPR technologies can take to solve a genetic condition.

Beam and Editas have different methods for "fixing the car." But the goal is the same: cure disease of genetic origin.

The thing for us to keep in mind is that the entire industry is effectively a greenfield opportunity. In other words, this is an entirely new market. We are watching it form before our eyes.

And our portfolio companies – including Beam – are the largest players, shaping it on their terms.

These companies have the technology to devel-

op a cure for every single human disease caused by genetic mutations. And there are more than 6,000 known genetic diseases that have no cure or therapy today. The size of the opportunity is in the hundreds of billions of dollars at least.

How Genetic Editing Works

Before I go further, I wanted to provide a quick refresher on genetic editing technology so that we can understand how it is used and why it is so powerful. This will be familiar to longtime readers. But for those just joining us, we should be sure to read on. This will help us better understand the difference between a CRISPR-based approach and a base editing approach.

First, we should understand the scope of the problem that genetic editing technology is addressing.

As I mentioned above, there are 6,000 diseases caused by genetic mutations. Worse, 95% of them have no approved therapy or treatment. To understand the scale of the problem, consider the following:

- More than a million babies are born with a chromosomal abnormality each year.
- More than five million babies are born with a genetic disease or major birth defect each year.
- Birth defects or genetic conditions cause more than 20% of infant deaths.
- About 10% of adults in hospitals are there due to genetically related problems.
- About 30% of children in hospitals are there due to genetically related problems.

Genetic editing technology has the potential to solve all these problems permanently by fixing the "typos" in our genetic codes that cause the conditions.

Here is how it all works:

To start, both a CRISPR-based approach and a base editing approach begin by creating a guide RNA. The guide RNA is exactly what it sounds like. It finds a specific segment of DNA, a precise location that needs to be edited by the gene therapy.

What makes guide RNA so incredible is that it can search all three billion base pairs in our genome and find the precise spot where a mutation exists. It is like finding a needle in a haystack.

Guide RNA

Source: Editas Medicine

In the picture above, the guide sequence is the target-seeking guide RNA, and the yellow DNA strand carries the corrected or desired DNA.

Once the guide RNA is developed, it is combined with a nuclease, a protein that is used to edit DNA. The most common CRISPR-associated protein is Cas9, but there are many others, including Cas12a, CasX, and Cas13. Different proteins are optimal for specific therapeutic applications.

Example of a CRISPR Nuclease

Source: Editas Medicine

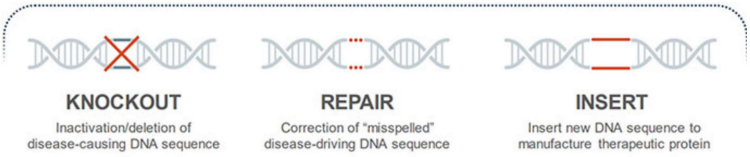
Above we can see the guide RNA (orange) with its therapeutic payload (yellow) and the nuclease (gray), which breaks or "cuts" the double-stranded DNA (light blue and dark blue).

This is such an elegant technology. To be able to search, find, cut, and replace an unwanted mutation amid three billion base pairs is just awesome.

And here's the thing... it just works. It demonstrates specificity, efficacy, and precision.

This CRISPR technology can be used in a few different ways. And depending on the therapeutic approach, different techniques are used.

Different Techniques of CRISPR Genetic Editing



Source: Intellia Therapeutics

In some cases, it is desirable to inactivate or entirely delete a genetic mutation that is causing a disease. This is often referred to as a knockout.

In other applications, the goal is to simply correct a genetic mutation. CRISPR is used to cut the DNA and correct the misspelling of the DNA sequence. This approach repairs the DNA sequence to the way that it would have been without the unwanted genetic mutation.

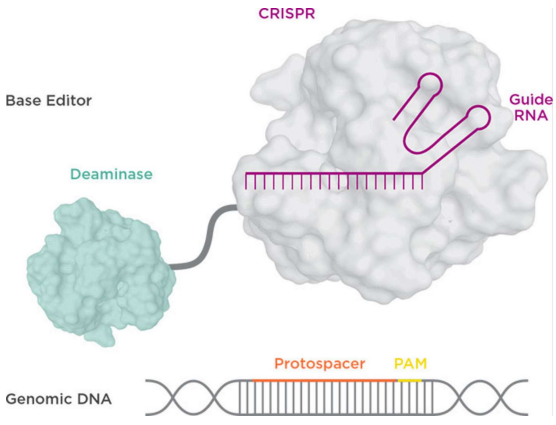
And at times, inserting a new DNA sequence is necessary to get the body's DNA to produce the right kind of proteins.

Again, none of these approaches is better than the others. Depending on the genetic mutation, the most effective genetic editing technique will be deployed. And that's where Beam Therapeutics and base editing come into play.

Base Editing

As I mentioned before, base editing uses CRISPR technology – specifically, the guide RNA – to find the right target amid the three billion base pairs of DNA. The base editing approach makes a small modification to the CRISPR-associated protein, which modifies it so that it doesn't "cut" the double strand of DNA.

Beam's Base Editing Technology



Source: Beam Therapeutics

In addition to the modified CRISPR-associated protein and the guide RNA, Beam tacks on a base editing enzyme, like a deaminase, which is the key to carrying out the desired chemical modification of the target DNA. A deaminase is an enzyme that

is capable of removing an amino group from a molecule.

In other words, it can rearrange the atoms in order to change the letters of a base pair of DNA. While this might not be intuitive, the picture to the right may help us visualize how this happens.

On the left is the whole base editing therapy with the guide RNA (purple) attached to the precise target DNA strand (dark gray). The deaminase (green) chemically alters the precise location in the DNA strand to change one letter to another.

What does that mean precisely?

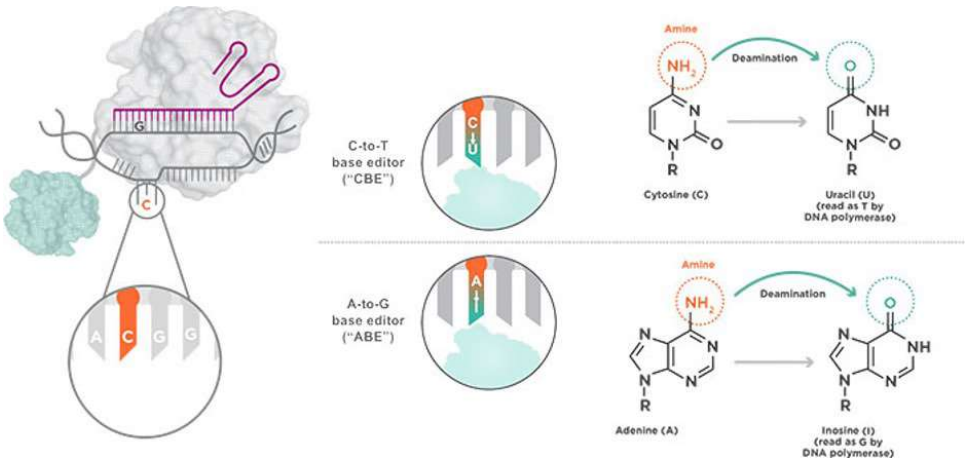
For those of us who remember our biology, we know that DNA strands are built on four types of nucleotides. They are...

- **C**ytosine
- **G**uanine
- **A**denine
- **T**hymine

We don't have to understand in detail how these nucleotides interact. But what we need to understand is that nucleotides need to be combined in the correct order for our DNA to function correctly.

Beam precisely transforms an incorrect nucleotide into a correct one. It is correcting a "typo" in our genetic code.

Base Editing in Action



Source: Beam Therapeutics

Beam has developed two different kinds of base editors:

- One capable of changing a C to a T
- One capable of changing an A to a G

Both editors function the same way.

So what applications are optimally suited for base editing?

Base editing is designed to correct "point mutations." Point mutations are the most common class of genetic mutations that cause human disease. Roughly, over half of all known mutations are point mutations. Just a single genetic mutation is responsible for untold suffering with no known cure.

And Beam's two base editors can address about 60% of known point mutations. The scale of the opportunity for Beam Therapeutics is so large that one company can't address each possible therapy. That is why there is so much room for multiple genetic editing companies in the market.

In fact, I would argue at this stage, the more high-quality companies the better. This might

seem counterintuitive. On the surface, it might appear that genetic editing companies are competing with one another. But in reality, the opportunity is so vast that there is plenty of room for everyone to have incredible success.

And the world will benefit from this greatly. After all, 6,000-plus genetically caused diseases need to be cured. It will take a lot of bleeding-edge teams to make that a reality.

Beam's Pipeline

Let's have a look at what is in Beam's therapeutic pipeline.

Beam's most advanced lead candidates are focused on hematology (blood-related diseases) and oncology (cancer).

The blood diseases are sickle cell disease and beta thalassemia. These were logical choices, as both diseases are caused by point mutations that are very well understood and therefore easy to target.

CRISPR Therapeutics has already had great success in early Phase 1 clinical trials for both diseases. It is too early to tell, but Beam's base editing approach may even be more successful than CRISPR Therapeutics' CRISPR-Cas9 approach to curing these diseases.

As for oncology, Beam is focused on a CAR-T (chimeric antigen receptor T cells) therapeutic approach to cure T cell acute lymphoblastic leukemia and acute myeloid leukemia.

Our T cells are a form of white blood cell that is critical to our immune system. CAR-T therapies help modify T cells so that they recognize cancer cells. The T cells then target and destroy those cells. It is like training the human body to eliminate cancer by itself.

To give us an idea of how much a successful CAR-T therapy would be worth, we can look at a previous transaction in the biotech industry. In January 2018, pharmaceutical giant Celgene acquired Juno Therapeutics for $9 billion explicitly for Juno's CAR-T therapeutic pipeline.

Different Techniques of CRISPR Genetic Editing

DELIVERY	THERAPEUTIC AREA	PROGRAM / DISEASE		APPROACH	RESEARCH	LEAD OPTIMIZATION	IND ENABLING	PHASE I/II	PIVOTAL
ELECTRO-PORATION	Hematology	BEAM-101	Sickle Cell Disease Beta Thalassemia	Fetal hemoglobin activation					
		BEAM-102	Sickle Cell Disease	Direct correction of sickle-causing mutation					
	Oncology	BEAM-201	T-cell Acute Lymphoblastic Leukemia	Multiplex silenced CD7 CAR-T					
		Acute Myeloid Leukemia		Multiplex silenced CAR-T					
NON-VIRAL (LNP)	Liver Diseases	Alpha-1 Antitrypsin Deficiency		Precise correction of E342K					
		Glycogen Storage Disorder 1a		Precise correction of Q347X					
				Precise correction of R83C					
		Undisclosed		Multiplex editing					
VIRAL (AAV)	Ocular and CNS	Stargardt Disease		Precise correction of G1961E					
		Undisclosed		Precise correction					
		Undisclosed		Gene silencing					

LNP = Lipid Nanoparticle; AAV = Adeno Associated Virus; CNS = Central Nervous System

Source: Beam Therapeutics

Both Beam's hematology and oncology therapies are going to be delivered ex vivo (outside the body) using a method called electroporation. Electroporation might sound complex, but it's not.

Cells are taken from the patient's body, and an electric field is applied in order to increase the permeability of the cells' membranes. This allows the cells to absorb the therapy more efficiently and effectively.

Once the electric field is applied, Beam can deliver the base editing package directly to the cells to perform the desired edits. Once the edits are completed, the cells can be returned to the patient in order to cure the disease.

An Exciting Future for Beam

Beam has several promising therapies – all using electroporation as the delivery method – that are currently being optimized. And Beam's executive team has referred to a "wave" of investigational new drug (IND) applications expected to begin this year.

When IND applications are approved by the Food and Drug Administration (FDA), biotechnology stocks tend to move higher. It means that the therapies have shown great promise in preclinical trials and warrant testing in humans.

Given that Beam has already had great success in its preclinical work editing human cells, I am confident that we'll see the first of these applications soon.

And back in February, Beam announced a common stock offering of 2.8 million shares to certain institutional investors at $93 per share, which will generate total proceeds of $260 million. This will help Beam raise the capital it needs to advance its lead therapies deep into the FDA clinical trial process.

And get this, one of Beam's biggest successes to date happened at another biotech company. In June 2020, Verve Therapeutics presented results from the very first trial of base editing on non-human primates at the meeting of the International Society for Stem Cell Research.

The results were incredible.

Verve's goal is simple. It wants to develop a one-shot genetic editing therapy for heart disease. It used base editors to target two genes that exist in both humans and monkeys (PCSK9 and ANGPTL3). Years ago, scientists discovered when these two genes are disabled, the lifetime risk of coronary artery disease is reduced by 88% and the lifetime risk of heart attacks is reduced by 34%.

Here's where it gets interesting.

When Verve applied the therapy to 14 monkeys, it witnessed an unbelievable change. In the seven monkeys that received the ANGPTL3 base editor, the monkeys' blood triglyceride levels fell by 64% and LDL (bad) cholesterol fell 19%.

And in the seven monkeys that received the PCSK9 base editor, the monkey's LDL cholesterol levels fell 59%.

Not surprisingly, Verve's CEO, Sekar Kathiresan, when discussing the outlook for Verve's base editing program on the back of these results commented, "We're quite confident." Rightfully so.

So what does all of this have to do with Beam Therapeutics?

Well, all of Verve's technology was licensed directly from Beam. Beam owns the foundational intellectual property for base editing. If Verve or anyone else wants to use base editing as a therapeutic approach, they have to come to Beam.

This is incredible for Beam. Beam can't possibly pursue every disease at the same time. So it will license out its technology so that other companies can investigate different diseases. And when successful, a royalty stream will flow back to Beam… at 100% gross margin. Pure gravy.

The People Behind the Story

As usual, there is always more to the story, and this time it has to do with the scientific founders…

Editas Medicine was founded by a team of scientific rock stars – Feng Zhang (biological engineering), George Church (genomic sciences), Keith Joung (pathology), and David Liu (chemistry). All four graduated from Harvard and maintain ties in a variety of capacities. Combined, they are an incredible team that formed one of the world's leading companies in genetic engineering.

As I have written on many occasions before, I believe that Editas has the most valuable foundational patents for CRISPR technology in the industry. This technology is worth billions of dollars.

What's the connection between Editas and Beam? Three of the four scientific founders also founded Beam Therapeutics – Zhang, Joung, and Liu. And it was Liu this time who brought the incredible discovery of base editing to Beam.

As a chemist, Liu was perfectly suited to tackle the challenge of making edits to DNA without actually cutting. He and his team were the ones that discovered the ability to chemically replace one base letter with another. For this revolutionary discovery, Liu's work was recognized by Science Magazine as one of the scientific breakthroughs of 2017.

And Liu believes that base editing might even offer a solution to genetic hearing loss. In June 2020, he and a team published a study where they managed to restore hearing loss in mice that was caused by a genetic mutation. That makes this another promising field of work for Beam to explore.

Beam was also backed by two of the most successful venture capital firms in early stage biotechnology, ARCH Venture Partners and F-Prime Capital. ARCH is so sure of its investment in Beam Therapeutics that it owns 17% of all outstanding shares across two separate venture capital funds. It appears that it wants to share the future gains in two funds rather than just limiting the gains to one.

Why Now Is the Perfect Time to Invest

I want us to get in now because of what is happening in the genetic editing industry. Editas is on the verge of releasing Phase 1 clinical trials for its therapy for LCA10, a genetically caused form of blindness. And CRISPR Therapeutics and Intellia are pursuing very promising therapeutic programs as well. When these companies continue to release positive results, it takes the whole universe of genetic editing stocks higher.

And remember that "wave" of IND applications – and FDA approvals for clinical trials – that Beam is setting itself up for this year? Well… I want to make sure we invest ahead of any positive news. All it takes is one piece of news to make the stock start to run.

Let's make sure we get in before that happens. After all, we're in this for long-term, triple-digit gains. And Beam, just like our other genetic editing companies, has 5–10x profit potential.

Action to Take: Please refer to our model portfolio for the most current recommended buy-up-to price for **Beam Therapeutics (BEAM)**. Be sure to use a limit order when placing trades. For the time being, we will hold BEAM with no stop loss. Always remember to use rational position sizing.

Risk Management: We will be holding this position without a stop loss. So let's remember to always keep our position size rational. And remember, I never recommend going "all in" on any one investment.

Regards,

Jeff Brown
Editor, *Exponential Tech Investor*