SHORT BRIEFINGS ON LONG TERM THINKING – EPISODE 19

BREAKING THE BIOTECH MODEL

MB – Malcolm Borthwick

JA – Julia Angeles

MB Hello and welcome to Short Briefings on Long Term Thinking. Thanks for joining us. I'm Malcolm Borthwick, editor of Intellectual Capital at Baillie Gifford.

Throughout history, the world's finest scientific minds have struggled to develop effective vaccines to cure plagues and pandemics, but not this time. Without wishing to detract from the terrible suffering and death toll of Covid-19, the virus has highlighted the spectacular advances in scientific discovery.

It took four days to sequence the genomic code and design the vaccine for Covid-19. Yes, just four days. So, what are the implications of this for finding cures for other diseases? I'm joined by Julia Angeles, who's co-manager of Baillie Gifford's Health Innovation Fund. But before we start the conversation, some important information. Please remember that as with all investments, your capital is at risk and your income is not guaranteed.

And this podcast has been recorded during Covid-19, so Julia and I are both at home, as opposed to in the usual Edinburgh studio. Julia, thanks for joining us.

JA Thank you, Malcolm. It's a pleasure to be at home.

MB Let's start with that four days, because that's an extraordinarily short period of time. Not long to find a solution and design a vaccine. Talk me through that.

JA Actually, it took us just two days to read the blueprint of the Covid-19 virus, and two days to produce a vaccine that's actually now in humans. And the reason why it became possible is because we had all these technologies already being proven and working in real life. So, to read the genome of a virus, we use a technology called genome sequencing. This is technology produced by companies, like Illumina.

We have already been experimenting with this tool for more than a decade, and continuously reducing cost and increasing the precision of the technology. And because of these ground-breaking advancements, we could read and analyse the genome of the virus in such a short time.

Some of the leading vaccine technologies, which are already on the market and saving many lives, are based on entirely new approaches, which rely on technologies like messenger RNA. What messenger RNA does is it codes for certain proteins within the virus that, in turn, have been expressed in our bodies for the immune system to recognise and produce antibodies against it.

So, a lot of it looks more like digital technology, rather than anything we know from the life science industries from the past. So, this has genuinely been a transformative shift in the way we think about a vaccine, and this is also why it allows us to come up with a solution in such a short period of time.

MB And what are the implications of messenger RNA for other diseases?

JA The applications are very broad. But if we take the closest to now, what most people understand of how messenger RNA works in the vaccine space, the next big application is to apply the same concept to oncology. So, companies like Moderna, Biotech, and CureVac, these three companies are leading the space within messenger RNA, and all of them are working on vaccines for cancer.

When patients are diagnosed with cancer, we can understand what sort of profile this cancer has. And cancers have their own signatures, genomic signatures, based on the mutations that took place in cancerous cells. And then we can take this information and translate it into the biomarkers that trigger the immune system to recognise a cancer cell and kill it.

So, again, we leverage the role of the immune system to kill the cancerous cells, and we also use a personalised approach where every patient is treated with an individual approach, where every cancer gets sequenced and analysed. Then we programme messenger RNA to reflect the signatures of the patient cancer. So, this is a genuine paradigm shift in the way we approach it. This is a genuinely personalised approach. So, this is the closest to the vaccine space.

But another application could be if, for example, in rare diseases, very often, we are missing certain proteins that perform important functions. And what messenger RNA can do is programme that missing protein to be delivered in the right place in the body, so the body starts producing these proteins. Suddenly, it's a very natural approach. This is the way biology works.

And what these companies have done, they have hijacked the biological process, and it's as close as you can get to it. So, as I say, in a way, there are no limitations on how messenger RNA can be used.

MB It's interesting because messenger RNA has been around for a while, hasn't it?

JA It has. Actually, the first company who moved into the space was a German company called CureVac, but they've been much slower than Moderna in bringing drugs to the market. So, as I say, the idea is not new, but it's just executing on that idea is really, really difficult. Because as soon as you inject messenger RNA into the human body, the immune system would recognise it and destroy it. So, that

way, I keep referring to the delivery mechanism, which has been fundamentally crucial to solve that challenge, in order to make messenger RNA into a drug.

MB That's an interesting point you raise about execution and the ability of companies to execute on these ideas. How important is that when you're looking at the possibility of investing in companies, their ability to execute?

JA This is one of the very important aspects for every investment we make. Because you can have an amazing technology, but if you don't have a management team that has a long-term vision and is also able to attract capital and talent, it's almost irrelevant what technology you have in your hand. And now, given the pace of technological innovation, you will be very quickly displaced if you don't move fast and you manage to attract capital and talent.

For example, with Moderna, we saw at the early stage that they managed both capital and the people side extremely well. They have some of the best talent on both the science side, but also, they managed to attract the best talent on the manufacturing side, which is also extremely important for scalability of this technology. And another important aspect, of course, is capital.

Moderna managed to raise billions of dollars prior to going public, which is also important in the process of a company's evolution. Because as companies stay private, they are in a much better place to experiment and make mistakes, having no pressures from external investors. So, we really think that the more companies manage to raise, at the early stage, the better in the long term.

MB As you've mentioned, Moderna is a great example of where healthcare and tech intersect. And also, our ability to use and make sense of data, which is vital. Give me some other examples of companies where you see that interaction between healthcare, data, and tech.

JA Of course. One of my favourite examples is a portable ultrasound machine. As most people would know, currently, ultrasound is performed in the hospitals, in a dark room with a massive machine, and it will be operated by a person who has many years of education. Because the technology is really sophisticated, it takes a skill to acquire the image and also a skill to make an interpretation. It's quite an expensive diagnostic tool.

For this reason, currently, two-thirds of the world don't have access to ultrasound technology. And this is really quite a sad statistic, because this tool is incredibly powerful for diagnosing many, many diseases. It very much remains the case that most of the world don't have access to it. Butterfly Network has come up with a portable device that solves all the challenges that stop that technology from being accessible all around the world.

So, one is cost. Another one is usability. The cost of their device, which is the size of the palm, is $2,000, which is a hundred times cheaper, compared to a traditional machine. So, this is already a transformation. But even more exciting, they managed to integrate machine learning tools in both the acquisition of the image and the interpretation.

So, the reason why Butterfly was able to achieve such a device is because they reinvented the underlying technology of ultrasound. They put it on a chip, the same technology that powers our phones and our computers. And as we know, if you put something on a chip and you start scaling up, the costs just decrease exponentially. So, this is one aspect that's allowed them to make such a tool.

In addition, all data is stored in the cloud, processed in the cloud, and then you use machine learning to make interpretations. So, you're using all these technologies that we're using also in other industries, and when you bring it to healthcare and you combine them in a very intelligent way, you come up with entirely new ways of doing things, entirely new ways of practicing health.

And we are already seeing that this, too, is transforming the patient care in both developed countries, but even more importantly, in developing countries, that will be leapfrogging from those big machines directly to something that is actually much more powerful than what we know in the developed world.

MB How did you get interested in health as an investor? Have you always been interested?

JA I was always interested, even before becoming an investor. I studied economics, and before choosing to go for economics, I was considering studying medicine. But, for some reason in my 20s, I decided that economics is probably a more useful science and I can do a lot of good things with that. And then you study economics and you realise there are a lot of theories and very little application to real life. But still, of course, it teaches a lot of interesting methodologies and mental models.

And healthcare, for me, has always been a fascinating area because I always tried to understand how the human body works, and then you start learning how little we understand, and then it became a challenge. And when you see what's happening now with the proliferation of all the tools that really help us to understand, actually, how we function as very complex human entities, then that is probably the most exciting time to look in that space.

Maybe I was lucky not to study medicine in the traditional way when I started, instead of looking at healthcare at this stage.

MB Because there's so much more to learn, especially about areas like the brain, where our understanding, at the moment, is probably fairly limited.

JA Indeed. And the brain really has been the last frontier that's been so difficult to address for scientists and for companies, to come up with effective drugs against diseases like Alzheimer's. And this is for a very good reason, because to get access to the brain and study it has been impossible. We can only study the brain in dead people.

What's really fascinating, over the last decade, is that we've had a proliferation of new technologies and new tools that give us insight into the brain. One technology linked to that is imaging. We have a variety of imaging approaches, so we can

actually analyse the brain. But another one, which is really fascinating, is stem cells.

We can use patients' stem cells, who have Alzheimer's for example, to trigger their cells to be disease neurons, and then we can study those neurons in a petri dish. And we can even experiment on what sort of drugs could possibly work to invigorate the neuron. And this has been transformational in the way we can study the brain disease, but, also, potentially finding treatment for brain diseases.

And then, of course, there is another massive challenge. So, one is to understand actually what's driving diseases, but another one is getting access to the brain. And as we know, there is a blood brain barrier for a good reason, to protect our brain from invaders, but it also protects the brain from good things, something maybe we would like to supply the brain with.

And that challenge has been there for decades, and only recently we've started making some big steps towards finding solutions on how we can bypass that challenge. And companies like Denali are really making a lot of progress in addressing the blood brain barrier, and they have already demonstrated, through their technologies, that they could get through that challenge. So, this is really exciting.

On one side, we start understanding better what drives brain diseases, but on the other hand, we also have tools to get access to the brain. So, this will be transformational for the brain biology in the long term.

MB That's a great place to end it. Julia, thank you so much. It's very exciting, the developments that we're seeing in health innovation at the moment.

JA It's exciting, indeed, and we really think our job is so fascinating and we continue to be looking for these transformational companies. Thank you for listening to me.

MB You can find our podcast, *Short Briefings on Long Term Thinking*, at bailliegifford.com/podcasts, or subscribe at Apple Podcasts, Spotify, or TuneIn.

And if you enjoyed it, please spread the word. And in our next podcast, we'll be looking at ESG. How does Baillie Gifford view ESG? Is it just an extension of our long-term thinking? And how should we engage with companies to find solutions to society's challenges and drive progress?

That's in the next edition. And many thanks to Lord of the Isles for the music. The track we've used is called *Horizon Effect*, which is released on Permanent Vacation. And if you're listening at home, you're listening in the car, wherever you're listening, stay well and we look forward to bringing you more insights in our next podcast.

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