PODCAST TRANSCRIPT

AN INTRODUCTION TO SYNTHETIC BIOLOGY

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Burgers, skin care, designer handbags, contaminated water and of course, Covid-19 vaccines. These are just some examples of synthetic biology technology that's out there in the real world today. It's an area that's developing at a remarkable pace. At Walter Scott, our research focuses on companies, not themes. But there are often key trends such as synthetic biology, which merit a particularly deep dive. It's clearly an area with far-reaching consequences for businesses around the world, and we've been fascinated by the opportunities and risks it presents for investors today and in the future.

Katie:
Hello and welcome to today's podcast from Walter Scott on synthetic biology. I'm Katie Boyce, an investment writer at the firm, and today I'm thrilled to be joined by my colleague, investment manager Tom Miedema. Tom, great to be chatting with you today.

Synthetic biology, it's a pretty big topic, so let's get straight to it. Perhaps you could start by explaining exactly what you mean by the term.

Tom:
Hi, Katie. Thanks very much. Yes, happy to. It is a massive topic. If you typed synthetic biology into Google, you get all sorts of explanations for what it is. What I was trying to capture by using this term was really broad. Thinking about all of the ways that humans are able to manipulate the fundamental constructs of biology to achieve different outcomes. That could be in a healthcare setting when you're trying to kind of create a new therapy

using mRNA vaccines, or whatever it might be, or it could be in an industrial setting where you're trying to create a synthetic version of something that exists in nature, let's say spider silk or something like that.

Katie:
I think you've mentioned to me before about pineapple being involved in leather production, which we can come on to discuss later.

Tom:
Absolutely, we should definitely talk about that later. One example we've used quite a lot in this area is this idea of the cell as a factory, and then within that, the genes within a cell being a computer or a control system for controlling that cell. A cell, when you look at it, is just an incredibly flexible factory – it can produce an almost infinite variety of different things. It's got its own power station. It's just very, very complex and flexible. And then if you look at the gene, you can think of it as the computer. It's got an incredible amount of data in there. You can effectively code the genes to produce lots of different proteins in the cell. This is typically what the cell is manufacturing. I think that conceptual construct really can help to visualise it.

Katie:
Synthetic biology sounds relatively new but I gather it's been around for a lot longer than many people would think?

Tom:
I think you can think about it either in the very long term of history, you could think about it being around for 2,000 years and talk about Aristotle. The way that I tend to think about it is that it's been a phenomenon that's really kicked off in the second half of the 20th century. The 50s was a period where it became very active. From there, we have seen lots of different milestones and technologies coming together to create what we see today – the first synthesis of human insulin, the Human Genome Project, the ability to sequence DNA using the Sanger process, the mRNA vaccines, and a whole host of different kind of key breakthroughs.

I also think about it as a massive multidisciplinary effort in science. It crosses biology, chemistry, robotics, computer science – all of these things coming together to accelerate to the point where we have all these tools in place and can use this technology for the things that we're going to talk about.

I think at this point, it's worth noting we've been writing a paper on this whole topic. So, rather than dip into the entire history here, this is hopefully a reasonable teaser as to some of the things that have happened.

Katie:
Covid-19, the Moderna vaccine and mRNA really shone the spotlight on this technology but what sparked your interest?

Tom:
That was one of the factors but for me, it started quite a bit before then and was purely bottom up. Sometimes you can start off with the intention of getting into a project – at Walter Scott we can take all different avenues before we kind of get into these things – but here it was really company based. I started looking at a company called Sartorius Stedim, which is a bioprocessing equipment supplier, and I got very excited about the business model. It operates in an oligopoly. There are effectively four players in that market. It serves a very large, very profitable and growing industry. It has high single-digit growth already – hundreds of billions of dollars of revenue in that industry. One of the nicest factors is that once you sell your piece of equipment into a new drug product, you'll sell consumables into that broad drug product for the entire life of that product. And those customers are incredibly sticky because, once you are signed up, you're in the regulatory pattern for that product.

Then I started looking at the peers – I looked at Merck KGaA in Germany, Danaher, and some of the other peers in that space. From there, I followed the breadcrumbs and went further into the customer base for these bioprocessing equipment players. Here you're thinking about CDMO – these are contract development and manufacturing organisations. These are companies that outsource manufacturing of predominantly biologic drugs, and they've been gaining share significantly. They were the fastest growing customers of the likes of Sartorius and Merck. That was a really interesting space to me as well.

Katie:
It's a bit like the semiconductor industry.

Tom:
Yes. As you know, I've spent a long time looking at semiconductors so when I saw what was happening in that space, I immediately saw those parallels. When you look at semiconductors, there's been a long trend towards outsourced manufacturing because, as time goes on, it's harder and harder to manufacture the newest products and it's more expensive to build the factories. While it's not exactly the same, there are many parallels with what happened with semiconductors over the last couple of decades with what is happening in these new modalities of biologics right now.

Katie:
You've really immersed yourself in the whole industry, haven't you? I think you've met tons of companies and you've attended various industry conferences.

Tom:
That's one of the best parts of the job, right? You really get stuck into a topic. I've met with every company I could find in this space, globally. We've attended industry conferences.

Katie:
And you've attended academic conferences. I think there was one in Berlin you went to not that long ago.

Tom:
Yes. It was a really good conference. It was an mRNA conference in Berlin that was two days, and was almost entirely industry. I think I must have been maybe the only one or one of very few investors there. It was fascinating. It was basically scientists and people in the industry talking about what they're excited about – where this technology is heading, and that's way beyond vaccines, and what the challenges are. They're sharing problems and sharing solutions. It was just fascinating to be in and around the people that are really doing the cutting-edge science. I also read an embarrassingly large number of books on the topic and listened to many different podcasts, really trying to understand the science. And this has been over a couple of years, so it has been a steep learning curve. I am by no means a world expert, but I have done a lot of work in this space, which I've really enjoyed.

Katie:
The most obvious examples lie in healthcare, don't they? Perhaps you could talk about that.

Tom:
These technologies have been used in healthcare for a long time already. From simple biologics, and I think insulin would be the biggest example there, to more complex biologics, which are the backbone of things like cancer therapy and immunotherapy for a lot of the big pharma companies. But now what we're talking about is a whole host of different, what they call, modalities – things like mRNA, things like peptides, things like cell and gene therapy.

You hear these referenced everywhere now. We're at the earlier innings of these, where there are a couple of products launched in these different categories. But these are going to be really big technology platforms in healthcare going forward. Think about them as a whole swathe of tools that very clever scientists are going to use to try and attack some of the really complex problems that we still face.

Katie:
And, within that space, cost is often the thing you read or hear about most.

Tom:
Yes, I think cost is a perennial long-term challenge in healthcare. Clearly, we're getting older, and society is getting less healthy over time. It comes with age and the costs are rising. I think these biologic treatments, while they are revolutionary and incredibly good for patients, they come at a price. So there is a serious challenge between how do you incentivise investment, how do you incentivise innovation for the pharma companies but, at the same time, make sure that these wonderful products are available to as many people as possible? I think that's going to be a big political debate. It's clearly a debate in the US and globally. The US is where it's more advanced today. But, ultimately, over the coming decades, we need to see this democratisation, reduction in cost, more biosimilars or the equivalent of generics in this space become available, such that more and more of the world population get access to these therapies.

Katie:
And beyond healthcare, there are real-world examples, too, aren't there?

Tom:
That's probably at an earlier stage than in healthcare. Healthcare, it's the here and now, and the future, of course, as I mentioned, whereas in industrial settings we're a little bit less advanced. There's lots of hype around the pineapple leather that was mentioned earlier. It's a great example, but really we're at quite an early stage. There are lots of start-ups coming through, and lots of exciting articles about the potential but, really, we're quite early. That's not, however, to say there is not huge potential in this space. I think it will inevitably be a very, very large industry going forward. You are going to see synthetic versions of biologic products like the pineapple leather, or leather from other different sources, or like the synthetic meats. This is going to be a big area, but I think we're still in that experimental stage at the moment.

Katie:
But it's not just start-ups and new businesses, is it? There are established players seriously looking at this stuff. I think Hermès is one that's talking about it, with regard to handbags?

Tom:
I think that adds credibility to the whole space. You have lots of serious businesses like Hermès, like Christian Hansen, like Novozymes, like Givaudan. There are many, many examples of companies that are exploring this because it's pretty much inevitable that it will be very important. I don't want to get overexcited about it being something we're going to see in shops tomorrow. Now, you'll see some, but it's going to be a big deal, I think, 10 or 20 years down the line.

Katie:
Tom, that all sounds great but there must be some risks or concerns around some of this? Maybe it's being in Edinburgh, but I'm thinking of when Dolly the Sheep was cloned and it caused quite a debate around the ethics of such technology. Is that debate still ongoing?

Tom:
I remember that well. Every household was debating those topics and then it went remarkably quiet for a long time. It's almost certain we're going to have to revisit a lot of these ethical and moral debates because these technologies are so broad-ranging and have so many potential ways to be to be used. We are going to be visiting the moral debates that more typically have been part of your favourite sci-fi films. Those are going to be real debates and society

needs to take it very seriously because this technology is coming pretty quickly and we should really try, as much as possible, to get ahead of that, to have these discussions before the science goes ahead of society in that regard.

Katie:
Ultimately, from the research you've done, synthetic biology is a is a force for good?

Tom:
I think that's a fair summary but the caveat there is that we have to remember that these technologies can be used certainly for good, but also for ill. We need to think about things like biosecurity. That's going to be a big issue in this area. Governments need to think about that carefully. We need to think about cost. We mentioned already that you need to think about safety so it can have regulatory pathways, making sure that we are as certain as we can be that these new products are safe for patients.

The ethics that we talked about as well – there are lots of areas that we need to be very cautious around. Hopefully, I'm somewhat balanced in terms of a view – definitely positive but also aware of the potential negatives that come with it.

Katie:
Cautiously optimistic.

Tom:
I think that's a reasonable way to put it.

Katie:
Tom, what happens now? How will this feed into your future company research?

Tom:
The really nice thing about this topic is that it's very relevant for investment. I've looked at other topics previously and it's actually quite difficult to find big and good investments at an early stage. Here, you've already got a very established market, lots of profitable companies and actually companies that we already invest in that are exposed significantly to this thematic.

In terms of investment thinking, I've spent quite a lot of time thinking about what areas are of interest based on what we've learned here. I think any company exposed to particular volume growth in this space is going to be very, very strong because we're at the early innings there. Bioprocessing equipment players are heavily exposed to volume. I'm talking about companies like West Pharma in the US, where they make stoppers for the vials that you use to administer biologic drugs. And if you're playing on stoppers, you're playing on volume in that space. I think these are interesting areas to look. I mentioned CDMOs – I think the outsourced manufacturing piece could be a really interesting area for investment as well. Those players are taking share. It makes a lot of sense. There are a lot of reasons why people want to move away from manufacturing their own product towards letting these big specialised players deal with that complexity. Also pharma companies, it can be a challenging area, but some have either a lead in the technology or have incredibly strong domain knowledge, big sales forces in certain areas, and they're going to benefit from some of these technologies.

The caveat is that these are going to be commoditised. There are going to be technologies that, ultimately, are available to everybody to use and innovate on. We have to be very, very selective in pharma.

I've talked a lot there, but I think there's going to be a lot of investment opportunity in this area. I'm excited for the next couple of years to continue learning more and picking out the niches that are going to be most interesting within this trend.

Katie:
Earlier, you mentioned you had done a lot of reading on the topic and it's clearly a huge area and massively technical. I just wondered if there was any entry-level reading you could recommend for anyone who's keen to learn a bit more?

Tom:
There are a lot of good books in this area. One I really enjoyed was *The Genesis Machine* by Amy Webb and Andrew Hessel. The reason I picked that one out is because, after having read a lot of different books and, as you say, there are a lot of different topics here, some are easier to get into than others, but that one really did a good job of summarising the space. And I read it relatively late on. I wish I'd found it earlier. So that's a really good one to look at.

The other books that are hard to look past are the Siddhartha Mukherjee books.

Katie:
He spoke at a conference in 2016. He wrote *Emperor of the Maladies* and *The Gene*.

Tom:
Exactly. He's had those two books and since he's produced another one called *Song of the Cell*. Those are all excellent, a little bit more heavyweight but worth the read for the comprehensive history and going through all the science.

Katie:
Great. Thank you very much for your time today, Tom.

Tom:
Pleasure.

Katie:
That's been a great insight into a huge topic. And I know you've written a paper on it, too, so we look forward to sharing that with our listeners very soon.

And to our listeners, thank you very much for taking the time today. If you have any questions on what has been discussed, please don't hesitate to get in touch. We look forward to talking to you again soon.

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