
HEALTH INNOVATION

Investing in exceptional biotech

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Before we start the conversation, some important information. Please remember that with all investments, your capital is at risk and your income is not guaranteed.

JT Welcome, all, to the first Health Innovation portfolio update. In this meeting, we're going to discuss some of the developments and news from the investment team within Health Innovation. As you're all hopefully aware, the team has been up and running now for just over three years. And we've attained our three-year track record in October. We thought, as we come towards the end of the year, it's time now to reflect back on the last six months or so, and talk a bit about what's been happening in the portfolio, what's happened in the team. And general updates of where we're finding those exciting names within Health Innovation.

To start with, one of the first questions that we'd like to address is about the portfolio and some of the companies within the portfolio. What companies have made surprising progress in the development of technologies or products in the last six months?

And obviously, Moderna has been in the news a lot recently. I don't know, Julia, whether you'd like to comment on how you think Moderna is progressing and what you think will happen to Moderna beyond Covid.

JA Thank you, Jack, for the question. With respect to Moderna, actually, there is not much change, I would say, with respect to the past six months. The company started executing really well from the beginning of pandemic, trying to deliver their solution to the current crisis. What we've really been surprised is how well the company has executed on the potential of messenger RNA, because this



technology basically was not tried in patients.

We didn't have a single medicine based on messenger RNA before Covid-19. And what was really remarkable is how company managed first to deliver their technology to clinical trials and then execute on clinical trials. And now it's about scaling up the manufacturing and trying to produce as many doses as possible to cover the world. Because we know the solution to this crisis has to be global.

For us, it is really encouraging is to see that the company continues to execute exceptionally well.

JT I think it's very interesting. Obviously, we've seen, unfortunately, with the next variant, a focus back onto Covid. But I think, as you said, it's a lot more exciting than that, the execution that they've been able to deliver upon. It continues to be a company to watch for the future and one that we're still very optimistic about.

Rose, I wonder if you can maybe comment a bit on Shockwave. It's one of our middleweight holdings, I guess. Maybe cover off what it is that they do and why you think that they're such an interesting company going forward.

RN Sure. Shockwave is a California-based medical device company. And they pioneer a new technology called intravascular lithotripsy. This technology treats calcified blood vessels using sonic pressure waves. And actually, as a technology concept, it's decades old. You know how we treat kidney stones? This is the similar technology used to treat kidney stones in many patients. However, Shockwave has tried to miniaturise the technology and use it to treat calcium in blood vessels.

It's an entirely innovative method, but it's actually based on a very proven concept. We have invested in Shockwave for over two years. And what's surprising is that the technology itself is incredibly safe and effective. And the company has made a lot of progress over the past couple of years to expand both the market opportunities to different types of blood vessels and arteries and also to accelerate the pace of adoption. And this is thanks to the efforts to unlock the reimbursement landscape in the US and also to accumulate more and more data and clinical evidence to prove the utility of this technology.

We are very excited about the prospects for Shockwave. And we think that the company has reached an inflection point in its growth journey. And the next five years could be even more fruitful.

JT I think it's interesting you say that they've reached an inflection point in their journey. What indicators do you as an investor do you look for within these companies that show to you that you think that their growth potential's unlocking or that there's a next step coming? Is there anything specific to Shockwave or more generally that you look for?

RN Yes. When we invested in Shockwave, we identified potential barriers to adoption that the company might be faced with. Some of those barriers to adoption include reimbursement. How can they get paid adequately for their devices, education and training for doctors and also scaling up the commercial salesforce? And we



identified those barriers to adoption, and we monitor them throughout our investment period.

And as we see, the company is putting more and more effort in overcoming those barriers to adoption and making real progress, for example, in terms of reimbursement. The company has recently got a transitory reimbursement for their medical devices in the US, for both the inpatient and outpatient settings. That is a real outcome that will increase the level of adoption among health systems and doctors.

Those are real testaments to the operational progress. We also see them executing very well and scaling up their commercial salesforce. And as we see, the investment phase is playing out. It makes us realise that the company is entering another phase of growth where they have reduced a lot of these barriers to adoption. And therefore, the next journey of growth should accelerate from here.

JT That's really useful and I think it helps to show that the investment hypothesis is a living, breathing being. It's a continual process that you're going through when you're making these investments into companies, and the continual monitoring of them as they change. Another area that's worth discussing in the portfolio has been obviously that not all the stocks always go up all the time.

Two names that are sitting as the bottom contributors have had a slightly more volatile ride recently, which would be Ambu and Novocure, which are more widely held across the firm, but have been in the portfolio quite a long period of time.

I think it'd be interesting to understand a bit about Ambu, what they do, and if there's anything that you've seen that indicates to you that anything has changed in the investment hypothesis.

What it is that they are doing that gives confidence to build that conviction to continue to own them?

JA Ambu is a Danish-based company that produces single-use visualisation devices. Think about single-use endoscopes. Devices that allow us to see inside the body and other just for diagnostic purposes or for procedures. For example, colonoscopy would be one of those. Ambu started by introducing the single-use devices, first introducing to the bronchoscopy, looking into the airways. And this was actually the first device that'd been single-use applied in that area.

And the key rationales for using single-use devices, actually, is very simple. It's lack of cross-contamination. We have already a lot of statistics and data indicating that using reusable technology leads to cross-contamination and in certain cases, to the death of patients. Single-use devices should **entirely** remove that risk. But also, what also in terms of value they bring in addition to lack of their cross-contamination, is there availability of devices?

Because it's reusable, very often, those machines spend time being maintained or being cleaned. And that means when patients need it, very often, patients don't have access to it. And with the single-use technology, availability also becomes



quite an important advantage. As I say, there are two important areas where they change the outcome for patients in terms of cross-contamination, but also availability for doctors and to perform better job for patients.

Ambu was one of the first companies introducing the device on the market and they've been shaping and creating this new market. The idea was when you start first with applying this technology into the bronchus, the airways, they start expanding the market by introducing - for example, looking into duodenum - applying it to colonoscopy. And anywhere in the body where we need this type of devices, Ambu could apply single-use technology.

What has been encouraging over the past five years is that the company's consistently been expanding its market opportunity and also executing in new areas. They started in airways, they now moved into ENT and urology. And the next big wave for them would be duodenoscopy. And this is quite a big and important area and also much more sophisticated. But the company is making really incredible progress in terms of first validation of the technology, making sure that doctors are comfortable. Regulators also are happy where technology is.

From what we can see, the overall market opportunity is expanding. The company is driving that expansion. The company also is the market leader, giving it scale and also knowhow in single-use products and therefore they have price leadership. There is really a very benign competitive dynamic. The market is growing. The company continues executing.

If anything, our excitement about the opportunity is actually increasing. There is nothing there for us to point out that we should be worrying and raising concerns with management. Actually, overall, the investment case became even stronger than a year ago, because there is more validation in new areas of application.

JT That's very useful. I think one of the things that jumps straight to mind when you talk about single-use is the environmental impact. Is Ambu doing anything on that or does the benefit of single-use, in terms of increased hygiene, outweigh in our view, any environmental impact, given the numbers of procedures that are carried out with their devices?

JA That's a very important question, of course. And immediate or quick thinking would probably infer that because it's single-use, it should be less environmentally friendly. But we shouldn't forget that reusable technology also requires a lot of energy for sterilisation and a lot of water also and chemicals. It's not entirely environmentally friendly, in the case of reusable. But of course, in the case of single-use individualisation, there is a large environmental impact.

The first area which the company's trying to address is what type of plastic they're using. That's the first area of focus. The next step for them to think about is recycling. Because, at the moment, those devices mostly are burnt. And then the next question is "what can we do to make it in much more sustainable way?" The company is certainly looking into those areas to decrease the environmental impact.



JT I think it's an interesting space. And obviously, it's a very complex problem, when you're thinking about the true impact of any product or any company. It's probably something we're going to discuss a little bit later on in more depth.

The other one, just to quickly touch on, would be Novocure, which is a pretty fascinating company, who have a very different approach to the diseases that they target.

I wonder if it'd be possible to describe briefly what they do and the investment case behind it. And whether, again, there's been any changes that have driven the slight depreciation in share prices or your current thinking as portfolio managers on Novocure.

MR Sure. Novocure is an oncology company that has developed a new way to treat cancer. It uses electrical fields to disrupt cell division. And that technology has been approved for use in glioblastoma, a cancer of the brain. The reason that you're asking me about it right now is that shares have been very weak. And shares have been weak on the back of revenues coming from glioblastoma being a little bit weaker than expected by investors.

This is really a short-term fluctuation that we would look past. In our holding, since we invested in Novocure, the investment case has progressed really encouragingly. The company has continued to expand the therapy to different countries and has obtained commercial coverage in seven key geographies now. It has expanded via a critical partnership with ZyLAB, another holding of ours, into China.

And crucially, it has continued to progress its clinical trials to add new indications, more indications that will be the engine for revenue growth in the future.

JT I think that's super helpful. It's one of these companies that's a little bit like pure science fiction. The idea of using magnetic fields to prevent the growth of tumours might seem a little out there. But obviously, there's very encouraging data that's been coming through and actual application on patients. That theme of science fiction becoming just science is another area that all three of you are dealing with pretty frequently.

And when we look at some of the new buys in the last six months, there's two companies there that fit that heading of 'science fiction becoming science' in some ways.

Exscientia is the UK company which has recently joined the portfolio in start of October. Would one of you want to just venture to try and explain what's probably quite a complex idea and why you think it warrants inclusion in the portfolio and what drove you to buy it on behalf of the clients?

JA As a team, we are really excited about the application of artificial intelligence in drug development. And there are many different areas where AI could really change the paradigm, the way we will develop drugs, by leading to much more effective medicines, personalised medicines and also leading to a higher chance



of success of bringing transformative medicine to patients. Exscientia is really playing into that excitement and the area where we think there are really going to be exciting opportunities.

The company is applying artificial intelligence in building small molecular drugs. The way the drugs develop at this stage, it's more or less in the sequential form. First, the drugs are optimised for efficacy. And then when we see that this particular molecule has a potential to be effective, then we try to manage it and shape in such a way it also doesn't cause severe side effects. And normally, you have to run compromises.

And that's why most of the medicines, even though effective, also have quite horrific side effects. With what Exscientia does, the AI actually allows them to optimise for different characteristics in parallel. They optimise both for efficacy and safety. And the way they do it, they apply all knowledge of biology and chemistry and they build small molecular drugs, atom by atom, while optimising for different parameters.

It's an entirely new way, actually, of developing drugs. Rather than taking drugs off the shelf and screening them and finding which one sticks, Exscientia is building one from the bottom-up, while taking into account what makes the best possible drug.

This is one way how Exscientia fits into the area of AI and drug development. But of course, they also use artificial intelligence in trying to understand the biology and understanding new targets that can be addressed with small molecular drugs. And those range from cancer to autoimmune diseases; a really, really wide range of diseases.

JT I think it's a fascinating idea that this in silico development can completely redefine the risk of developing new drugs in some ways. In terms of their progress now, where are they? And what are the key milestones that we'd want to see achieved? And how far away is it from being physically in patients or producing something that can go into patients?

JA It's still early days in terms of clinical trials. It has three drugs in Phase One. But having said that, the technology is really gathering momentum. We can imagine that over the next few years, the pipeline of clinically tested drugs is going to expand quite significantly, because this is the nature of the engine. As soon as you reach certain stage where you have enough data to start generating drugs, then, as Rose was talking about, we reach the inflection point.

Exscientia is actually at an inflection point of introducing more drugs into the pipeline. However, of course, it's going to take some time to get the patients. Because still, what we can't really change about the drug development process is that it needs to go through rigorous clinical trials and these take time. We can see there are still several years - five minimum - ahead before the drug is going to hit the market.



But having said that, you never know where else the company can apply it, if that technology is going to be useful solving the Covid crisis. It could reach much faster given the need. But overall, we still need some patience with this type of company to fully see the potential of the technology. But as I say, in terms of the productivity of the research engine, the results should be felt over the next few years.

JT And I guess the blue-sky case is that it could completely redefine the experience of patients who suffer from cancer. And I know that oncology is a bit of a theme that we've been looking at.

One of the other new buys that sits within that theme would be Lyell, which joined the portfolio about four or five months ago now. It'd be interesting to explore Lyell's approach to oncology and why that's different, and why it is exciting? What is it about Lyell and the way that they're doing things that makes it an interesting company to hold within the portfolio?

RN Lyell is a US company that is looking to reprogramme T cells in the immune system to develop curative therapies for solid tumour cancers. We know that cancer is a huge unmet need for patients. In the past few years, the field has seen significant advances in treatments for blood cancers coming from new therapies such as CAR T. However, these advances have not been translated into solid tumour cancers.

Lyell, through its research efforts, is looking into answering the key question, why do some of these advanced cell therapies work for liquid blood cancers, but not for solid cancers? What differentiates solid cancers from liquid cancers? And how can we reprogramme the immune cells to overcome these challenges that present to us by the solid tumours? The company has spent a lot of time diving deeply into the biology of cancer and of immune cells.

And they come to the hypothesis that one of the key challenges presented by solid cancers is the microtumour environment. That can exhaust the T cells in our body, making them incapable of killing cancer cells. The company has developed very innovative technologies to reduce or to stop T cells from getting exhausted and to maintain the T cells' stemness ability, which is the ability to rejuvenate, divide and to remain potent against cancer cells.

It's still very early days for Lyell. The company is still in the preclinical phase. However, we remain very excited about the prospects of the company. And if these technologies materialise, I think we can look towards truly curative cell therapies for cancer patients.

JT I think that that's a hugely exciting opportunity, albeit still maybe a little bit far away. When you talk about T cell vitality, it might be worth diving into what a T cell is and what it does? How would you explain it to someone who, like me, doesn't have much of a background in biology? And what roles do they play in fighting disease?

RN A T cell is a type of a white blood cell. When you think about the immune system, there are different participants in the immune systems and T cell is a key player. And there are many different types of T cells. There are killer T cells. They have



the ability to kill a cell that they think is foreign to the body or a cell that is dysfunctional, like in this case, a cancer cell. There are also memory T cells. These are the cells that have the memory of previous infections or previous viruses that have attacked the bodies, for example.

And there are, again, also T cells that can regulate the immune system. These regulatory T cells can actually dampen the immune system and stop it from overreacting. They play a very important role in the overall immune reaction of the body. And over the past decade, many researchers have come up with the realisation that cancer is a disease that occurs as a result of a dysfunctional immune system.

It's because the T cells somehow have lost the ability to supervise, identify and kill the abnormal cancer cells. What Lyell is doing, and many are doing, is just to reprogramme them so that they can do their normal jobs.

JT It's like harnessing a natural process and encouraging or supercharging it a little bit to go after a mutation with your own body, which is the cancer. Is that a fair summary, do you think?

RN Yes.

JT I think it's fascinating that we're now even talking about curative solutions for something like cancer, which has traditionally been thought of as, or it still remains, one of the biggest killers.

I wonder, in terms of what you're looking at now and the research focus going forwards, what are the main areas of excitement? What are you working on at the moment? And what technologies or innovations do you think warrant further attention over the next six to 12 months?

MR I think the exciting thing about now is that it's not a single technology, but a confluence of technologies that are making new business models possible. And each one will have our own areas of enthusiasm and focus. For me, I would say I've been quite captivated by a confluence of technologies that can allow us to understand biology in ever greater detail, eventually getting to the point where we can diagnose patients very, very early in disease progression on the basis of a single cell or a number of cells and interactions within them.

The most advanced opportunity there is probably in liquid biopsy. And you will hear a lot more progress coming from the field soon. This year has been the first year when liquid biopsy by GRAIL, which is now becoming part of Illumina, which we hold in our portfolio, has been approved in the US to be used as a diagnostic for many different types of cancer.

JT What does a liquid biopsy look like? If you were a patient, what does that screening look like? Is it a blood draw? Is it a biopsy of a tumour? What is it?

MR It's a big contrast to the diagnostics that we have now. Instead of an X-ray or a biopsy, which looks at physical changes within the body, a healthy individual can



come in and give some blood, have the blood drawn, with the technology being able to detect down at the cellular level changes happening within the body. It can detect the presence of cancer and it can also suggest where that cancer is located, even before we are able to diagnose it, even before we are effectively able to see it.

JT It brings forward the ability to intervene at earlier stage. And I think everyone who's listening to this will be aware of how important the role early detection plays within oncology in particular. It's exciting to hear that that's becoming a reality.

We spoke a lot about AI. But is there any other broader research focus or countries specifically or regions that we want to look at in more depth where we think things might be happening?

One of the questions that we've had quite frequently is about what's happening in China. Particularly earlier on this year, there was volatility in the market, more broadly in China, as the government changed its view of some technology companies.

It would be interesting to hear maybe your reflections on what you think the future of health looks like in China and where there might be opportunities there over and above or including the companies that we already own.

MR Meeting the rising demands for healthcare in China is an utmost priority for the Chinese government. We would be looking at areas where companies can radically transform health outcomes in China, where they can take costs out of the system and make patients healthier.

This is actually quite a big change to the healthcare environment that we have observed so far in China. A lot of the companies that we've observed, maybe up to even five years ago, were companies that would be following in the path of innovation that was created elsewhere. Either copying or following.

There is a very unique confluence of factors that has happened in the last five to eight years in China that is transforming that healthcare space and leading to a lot more innovation. We've seen the government adopt very decisive policies to really help shape and encourage innovation in the sector to help companies become more global. We have seen a lot of people returning from the west with experience in world-class companies and institutions, coming back to China and bringing all that experience.

There's now a very, very deep and well-connected talent pool, not just on the global arena, but importantly, within China as well. And we've also seen a lot of capital coming into China, both in the private and public markets. What you're getting are very well-capitalised companies with ambitious, talented people starting to compete at the global level to solve problems and healthcare challenges within China, but also globally. And those healthcare challenges within China are probably the biggest in the world.

We've come through the first wave of innovation, whereby companies built in



China would be bringing in innovative treatments into China and acting as a late-stage developer and distributor.

JT We talked about where they are now as being almost like a follower in some regards or copycatting and copycatting well. What might indicate that you're going to start seeing Chinese companies become global innovators, leading the space that they're in? Is that already happening or is the journey that we've seen with technology companies, for example, in China, instructive to the experience that we might see with health companies in China?

MR What we've recently seen was a very rapid development of the first wave of innovation in China. During this wave of innovation, companies acted as the gatekeepers to the Chinese market, serving as development partners for truly innovative treatments to bring into China or very rapidly developing equivalents. Not copying but developing equivalent treatments to the cutting-edge innovation that we're seeing globally.

That was the first wave of innovation. We're now seeing the second wave of innovation where Chinese companies are starting to lead the global development, where Chinese companies are starting to develop true breakthroughs. And that's down both to the talent and growing ambitions of the talent base. But it's also down to the strength of the capital base. We're now seeing companies that have participated in the first wave and became very well-capitalised.

These companies are now emphasising internal development, building out networks and relationships with academics or early-stage companies all over the world to really take cutting-edge innovation through themselves. But there's also really interesting development at a different level. We are seeing barriers to scale, barriers to entry for innovation starting to fall. And that's because a lot more development is down to technologies.

And we're starting to see companies specialising in providing those technologies that are enabling ideas to be translated into therapies.

JT Thanks for answering that. I think it's really interesting. We're in Edinburgh right now and China's a very complex place to understand what's going on sometimes as investors. How do you access what's going on within what can sometimes be or feels like sometimes it's a bit of a shut-off area? How important is the network that you've built in doing so?

JA I can have a go on that. I think what really helps us is Baillie Gifford's presence in China, in our Shanghai office. Our team there is really well connected with the local ecosystem. It allows them to build relationships and get to know inside-out what's actually happening. And as long-term investors, our approach is truly first to establish relationships, to understand long-term trends and who can we trust.

That's probably one of the major barriers investing in healthcare companies in China, really identifying founders who run business not in a dodgy way, but someone we can trust to be there in ten, 20 years' time. And this is a real problem.



We're actually in a very privileged position to be able to do that through our network of people who have really strong reputation and who have credibility in the industry.

The next step for us is explore what we can do as investors to help to support the growth of innovative companies in China. And it's something we have plans for in the future to do together with our Shanghai office, to do a roundtable and invite the best minds in Chinese healthcare and really have a conversation with them, to explore about the future opportunities and how we can help.

JT Thanks, Julia. I think it's interesting to see how a lot of the lessons we've learnt from being involved with companies like Alibaba and Tencent as a firm can translate across. Particularly the strength of physically having people within Shanghai and how closely we're integrated. I guess the other layer is to think about how the team has been changing over the last six months.

I know you have three new analysts who've joined the team now, but also Maria who's joined on the impact side. What's changing within the team and how will these new members impact in what you're able to do? Is it purely in terms of horsepower and being able to look at these new companies or is there anything changing within the framework of how you think?

JA Maybe something you forgot, Jack, to mention is our Artificial Intelligence Team, which is fully dedicated to the Health Innovation Strategy.

The way team is growing is all about making us better investors and to enable us to do the best job for our clients. That means identifying all these exciting companies and getting them into the portfolio as early as possible. And all we do is really to enhance our capability as investors.

When we speak about the new analyst on the impact side, and ESG, we truly believe that those parameters are going to be fundamentally important for our investment process. For companies maximising the impact on their innovation, maximising access, that should lead to more attractive market opportunities and better investments. We generally see the huge correlation between this work and investment.

And with respect to AI, of course, we really try to automate every single task that can be automated on our side to really release our time to focus on more value-added tasks. Everything we've done in terms of the team expansion is to enhance the investor's capability to do the best job for the clients.

JT I suppose it signals the firm's commitment to this, and the idea generation that comes from within the strategy, and pushes out more widely across the firm in terms of almost doubling the size of the investment team. And if you include the AI team, it's tripling in terms of actual people working on the strategy.

I wonder in terms of how the philosophy has changed, has there been any change in thinking?



I know you published a paper earlier this year on how you think about biotech companies. But what were the key lessons and takeaways from that in how you think about them? And what really drove those lessons?

RN Since we started the strategy in 2018, we have been fine-tuning our process framework, in particular, how we identify and invest in exceptional businesses in the field of biotechnology. We have developed the framework now, boiling down to a few key fundamental factors that we think can really contribute to higher chances of success for companies in this field. Those key factors are science, people, capital and an element of luck.

This framework is aimed at helping us narrow our focus when doing investment research, answering questions that really matter for this type of business. For example, in the area of science, we really focus on three components of the science. Is it credible? Is it differentiated? And is it scalable? We aim to identify companies that have scalable technologies that can allow them to repeat success time and time again.

And for us, that is a very important criterion. Because we believe that those that can repeat success over the long term have higher chances of becoming an outlier, both in terms of the medicines and the impact they can bring to society, but also in the financial returns that they can bring to shareholders.

JT I think it's interesting because it's a very different approach from a much more binary outlook on the chances of success. And it's also interesting to see that the philosophy is iterative in learning from the experiences in the past.

Other area that I'd like to delve into a little bit would be around how we think about the impact that you have as investors, particularly as ESG is front of mind for everybody.

It'd be interesting to hear your high-level thoughts on what the future looks like and how we can be impactful as investors, particularly in the health space.

JA Absolutely. As I mentioned before, we're truly committed to explore, and are already practising, the integration of ESG factors in our investment process. But of course, we think we can do better, and we can do more. For us, what we're looking for, especially in terms of what concerns climate, is really being ambitious with our companies, not just asking them to do what is currently agreed during the Glasgow meetings. But actually, to do more than that. Not just reaching net zero in certain time, but be carbon negative.

Can we actually start extracting carbon from the air? We'd like to push companies in that direction. One of the key philosophical attributes of our impact approach would be, "be more ambitious and do better than just what regulation asking you for".

Another area where we see the opportunities is bringing companies together to start collaborating on certain issues, rather than running solo approaches.



And one important area would be waste management. Are companies thinking about more radical solutions? And since we're owning similar businesses, the solutions could apply across those companies. Could we bring them together and make them work on those big challenges? And we'll keep identifying other important areas which we think are going to be really important for the climate and other aspects of responsible investing.

We'll engage with companies one by one very proactively on those questions. This is where we see, as investors, we can add value, where we have done the homework really to understand the key challenges and possible solutions. Then we can engage with companies in a very thoughtful way, but also drive collaborations within the industry, looking for those really radical solutions to problems rather than just trying to do patch work.

JT I think that's something that certainly jumps to the fore, you spend all your time thinking about radical solutions, not only in terms of radical cures and radical innovations, but how are we as investors can really maximise our impact.

I think we're pushing up against time. But thank you all, Rose, Marina and Julia, for joining us, and for giving us an update on how you're thinking.

And I hope that your clients find this a useful insight into what we're up to as a team and how we're thinking about the world going forward, as it continues to change almost beyond recognition, hopefully, over the next few years.

Thank you all very much and I look forward to speaking to you again soon.

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