Exchanges at Goldman Sachs

Gene Editing: The Future of Genomic Medicine & Biotech Investing

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Allison Nathan: This is Exchanges at Goldman Sachs where we discuss developments shaping industries, markets, and the global economy. I'm Allison Nathan, a senior strategist in Goldman Sachs Research.

Today, we're going to talk about gene editing which is an emerging and, in the words of our analysts, transformative biotechnology on the verge of rapid growth that has the potential to cure genetic diseases and defeat deadly viruses. A wave of innovation and M&A activity in the space is capturing investor attention.

So I've asked Salveen Richter, our lead biotechnology research analyst in the US, to join us to walk through the latest developments, the most promising applications, and the outlook for broader adoption.

Salveen, welcome to the program.

Salveen Richter: Allison, thanks for having me.

Allison Nathan: So let's start with the basics. For those who aren't as familiar with the space, what exactly is gene editing?

Salveen Richter: So gene editing is a versatile tool, and it's capable of making permanent, precise edits to the human genome. So I would think of it as a molecular scissors that really works to provide functional cures, and the spectrum of these different types of edits that can be made are growing as the technology evolves here. It is a revolutionary technology, as you mentioned. And we really do think it's poised to move the era of genomic medicine forward.

And what we've seen is, following the platform validation of other technologies such as mRNA in 2020, there's an increasing focus here on evaluating kind of the next frontiers in biotechnology, and we do view this as poised for rapid growth

Allison Nathan: And how does it differ from the related field of gene therapy?

Salveen Richter: The technology itself has the ability to address some of the challenges that are faced by gene therapy that you mentioned and also expand the addressable pool of disease areas, if not improve upon

options for these diseases.

So the difference, I would say, versus gene therapy and gene editing is that gene therapy is not always curative. And here you're talking about curative therapy, but you're also talking about the ability to expand upon different diseases and maybe target more than you could with just gene therapy.

Allison Nathan: So from what I understand, the potential applications of this technology are very extensive. So in your view, what are the most promising in the near term and maybe even over the longer term?

Salveen Richter: So I would think about it as right now we go after the easiest targets. So targets in the liver, targets in the eye, neurological targets. Those are just areas that we've seen proof of concept right now in moving forward in gene therapy. And so we'd expect gene editing to kind of follow suit, and they're starting with diseases of the liver. And then they're specifically looking at diseases where there's one defect or one mutation versus kind of a multiplex disorder where there's various mutations. Those will be probably what's next in the future.

And so we've seen nice success here outside the body or ex vivo as we've looked to sickle cell disease, beta thalassemia, and then cancers. And then we're starting to see approaches where we have in vivo gene editing, or in the body. And this was some of the big data that we saw last year where we saw improvement in a disease known as, a rare disease, known as TTR. And then also we've seen edits in the eye, which is a closed system. So that's where we're starting, and then we would expect definitely a revolution here in where this could go.

Allison Nathan: So just to understand that a little bit better, if you have a successful gene therapy for some of the diseases you just mentioned, ultimately, you are saying there's going to be a curative gene therapy treatment. How will this transform the way we treat these diseases?

Salveen Richter: So in the non-cancer settings, those could look to be functional cures. Or these therapies could look to be functional cures. In cancer, you could argue in certain settings it could be cure-like, but generally you're just talking really about extending life and improving benefits. So they won't be functional cures to the extent of

what we're seeing in the other disease areas or like a rare disease like TTR where you truly are removing symptoms and evidence of the disease.

Allison Nathan: So when you talk about some diseases where this type of therapy can be quite effective and curative versus cancer, what is the difference between them?

Salveen Richter: So the difference here is, outside of cancer, you can have a disease that's caused by-- let's say a defective gene. And so what you're doing is you're going into replace the defective gene with the correct gene. You're editing the gene, or you're just cutting it out. And so you're getting rid of the cause, and therefore you're curing the disease.

Cancer is just more complicated. You have mutations that have caused the disease, and so you're really going in to combat the disease itself. So there could be a case in a last-line setting that you get something that appears like a cure, which puts you in remission. But essentially it's going to be much more about improving life and expanding a disease-free state than it will be in the non-cancer

settings where you really are getting rid of the disease and the symptoms associated with it.

Allison Nathan: So we're hearing a lot about CRISPR technology. So tell us a little bit about what that is and how that fits into the gene editing picture.

Salveen Richter: So there are a bunch of gene editing technologies, and they've existed for a long time. The reason we hear about CRISPR/Cas9 to the extent that we do or just at this point just CRISPR-- because there are other aspects beyond Cas9-- is really that it is a very adaptive system. It's easy to use. So it's a tool and a technology at the same time. It's bacterial based, but really the extent of the ability to cure that we're seeing with this technology and now the innovation that's been driven around CRISPR is exciting.

Allison Nathan: So CRISPR in itself, just to be clear, is a gene editing tool and technology that's helping some of the advances you're talking about?

Salveen Richter: Exactly.

Allison Nathan: So last year, we did see the first successful in vivo proof of concept with the CRISPR technology. You mentioned in vivo being basically that you are editing within the body instead of taking out cells from the body and editing it externally. So what's the outlook for getting that type of technology into clinics? How far away are we from that? And what are you watching to gauge how far away we are?

Salveen Richter: So first, we're watching the ex vivo regulatory process here. So at this point, there are two companies that are partnered with an ex vivo, outside the body, CRISPR/Cas9, gene edited therapy. And they're guiding-- these companies are guiding to a year-end regulatory filing this year. So potentially an approval next year. And I think it's going to be really interesting to see what the FDA and even the European regulatory body do in terms of their want for approval here.

They did issue some guidelines last week where they detailed 15 years of follow-up data and so forth. And so we're going to get an understanding on the regulatory side here. In vivo is just a bit more complicated because you're editing in the body. There, the lead program is what we

mentioned, which is in that rare disease TTR. So the companies that are developing that drug are now going to move into a pivotal study and then move forward for approval there.

So we're here. These drugs are in the clinic. They're up for approval. And so it's exciting times.

Allison Nathan: So you just mentioned regulation. We've seen some important regulatory developments. We've seen the US Patent and Trademark Office recently decided that CRISPR technology is the intellectual property of Harvard and MIT after what was a long legal battle with other institutions. So will this ruling impact future regulation in the space? How it will impact the space broadly?

Salveen Richter: So it is possible that the decision you referenced will be appealed to the federal circuit and be in litigation for some time. Overall, we think the possible outcome is then the technology will just out licensed on a per-company, per-product basis. Ultimately, we don't think the ruling is going to have a major impact on innovation, per se. As we've seen with gene editing, there

are new technologies that are in development. This is going to be a very dynamic field.

And then, again, we'll get a better understanding from the FDA as what they need from their regulatory side. But from the IP side, we just do think, in the case of a ruling coming down and one company being awarded ownership of IP here or a university, that the rest of the companies will just pay a royalty.

Allison Nathan: So we hear so much talking about innovation. Machine learning. Artificial intelligence. They're making such important advances in so many industries. So how could advances in these types of technologies reshape the gene editing space and how research is done?

Salveen Richter: Yeah, it's a great question. I don't think we can ignore what's happening on the machine learning/AI side and how that's converging with biotechnology. And we actually have written a lot about that area.

Here, I believe it's going to initially be used within

manufacturing. But then also you're going to see these companies use high throughput screening to identify different CRISPR targets, and I think that's what's getting done now. And that's just the first-generation integration, and then we'll see more over time.

Allison Nathan: And so we talked about the regulatory side in terms of potential challenge, but you think it's going to be ultimately supportive of innovation. Are there other challenges facing the space that you're watching?

Salveen Richter: I think one thing we are watching is how to think about the long-term situation because what happens when there's so much innovation is that you have more and more companies entering this space and taking different technologies or improving upon the existing technology. So trying to understand where this field is going and who will ultimately be the winner is something we're sitting here trying to figure out. And ideally, you're just going to have companies bring in various technologies and then match the technology with the type of diseases or areas they're going into. But we're definitely watching this rapid pace of innovation, and that's something that is faster than we've seen in drug development in the past.

What we're watching aside from the IP situation and the regulatory situation-- And one challenge there that we are watching is the pricing models. If you're talking about a one-time functional cure that's going to come out at a high price -- and we've seen this now with gene therapy and it's going to play out for gene editing -- is the payor systems being able to absorb that.

And so here, there's going to be three approaches. Pay by performance, or value-based pricing. Or an annuity type pricing model. And so that is something we are watching because, at the end of the day, these drugs will have to get paid for to then be able to kind of fund the innovation aspect as well.

Allison Nathan: I know you've said before in conversations we've had that it's a challenge for a lot of these companies to have a curative technology because ultimately, again, it's a one-time payment. So can you just talk a little bit more, give us a little bit more detail about what this looks like from a strategic perspective for the companies who are funding this innovation?

Salveen Richter: When you think about Europe, they have a single-payor system and the US does not. And these payors are used to having really chronic therapies where you pay annually. And if they were to have patients that they cover switch to a different payor, then that would be fine because they would have just paid for what was used.

And here you have two issues that are playing out. One is the high price point where these drugs are priced over a million dollars in many cases. And then secondly, if you were to pay up front for that one-time payment and then your patient were to go elsewhere, how do you recoup those costs you paid for that long-term benefit? And so that is something that's very debated right now.

And I think in Europe, they've been looking at the value of these assets and debating that. They can manage the one-time payment model. In the US, it's just a bit more complicated with how we structurally are created. But I think the payors have to figure this out because there's more and more curative therapies. Hopefully that will come. And so they have to create some kind of model around this.

And it's much easier in a situation, even for the one-time payments, where there's a replacement cost. So if you're already paying a lot for an area like, let's just say hemophilia, and then there's a long-term duration or one-time payment but you're saving the health care system money, then that's much easier for them to swallow than a new drug curing a disease that has had nothing before.

Allison Nathan: So often when we talk about this gene editing space, ethical issues arise. You hear about designer babies and cloning of sheep. What is your perspective on the ethical issues?

Salveen Richter: So with regard to safety and ethical issues, which we're also monitoring here, one is the therapeutics applications of gene editing that we have discussed are really applied to somatic cells. And these are any cells in your body excluding sperm and egg cells. Germ-line editing would affect all cells in the organism, and these include eggs and sperm. And thus edits here could be inherited by future generations. So there's broad consensus among the scientific community that germ-line editing in humans should not be performed in light of

safety, ethical, and social considerations. So that's one area that's been monitored.

The other area is potential risks in the context of the edits. So here, we just want to make sure that we don't have off-target edits that lead to long-term side effects. And so when we're looking at these therapies, we're looking them in the context of the benefit-risk profile. So in a fatal disease, the benefit clearly would outweigh the risks. But we're clearly watching that profile and how that emerges, too.

Allison Nathan: Well, let's turn for a second then on the investment landscape behind all of this. We've seen a number of recent M&A deals and venture funding where big pharma has gotten very involved. How do you think this changes the outlook for moving gene editing into the clinic?

Salveen Richter: So I think, on one side, because of the data that we're seeing, the clinical data that we're seeing, ex vivo, in vivo, and the ability to innovate at the rapid pace that we can these days, you are seeing significant VC funding that's creating new companies with new

technologies and new approaches. And so when you think of the investment landscape, companies could choose to build the technology themselves. They could choose to acquire through M&A. Or they could partner.

And what we are seeing is that these companies are investing privately. They're choosing to acquire, but interestingly they're acquiring early next generation. And for the later stage companies, it might take validation, like even further validation or maybe understanding of the commercial landscape as well as the clinical regulatory landscape, for these parties or acquirers to then kind of step in maybe at a later standpoint.

So we are seeing monitoring from all the large companies, and they're aware of what's going on. And they're just debating how they make their move in this space.

Allison Nathan: So I guess let's just close in basically talking about the future. I mean, it really is early days for gene editing. But what are the developments you're watching? What are you most focused on as you see this space evolve?

Salveen Richter: We are watching base editing. This is-- So when we talked about the molecular scissors that is CRISPR/Cas9 right now, this would be a molecular pencil versus a scissors. And they can edit single nucleotides, so think about the four most common types of mutations or point mutations you could get. We're watching prime editing, which is more of a DNA search-and-replace word processor that expands upon gene editing. And then gene writing. So there's clearly a lot of next-generation approaches that are playing out over time.

Allison Nathan: Right. And the hope is of course we do end up with a lot of curative technology here.

Salveen Richter: Exactly.

Allison Nathan: Thank you so much for joining us, Salveen. This has been totally fascinating. I always enjoying talking to you about biotech and medicine. So thanks for joining us.

Salveen Richter: Thank you for having me. It's great.

Allison Nathan: And we'll also be diving deeper into

some distinct life sciences themes with Amit Sinha, partner and head of life sciences investing in Goldman Sachs asset management division, in the coming months. So make sure to look out for that episode.

That concludes this episode of Exchanges at Goldman Sachs. Thanks for listening. And if you enjoyed this show, we hope you subscribe on Apple Podcast, Spotify, Stitcher, Google, or wherever you get your podcasts.

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