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SPEAKERS

Chris Gibson, Vikram Purohit

V **Vikram Purohit** 00:04

All right. Welcome, everyone. Let's get started. This is a fireside chat with Recursion Pharmaceuticals. Very happy to have with me Chris Gibson, CEO of Recursion on the stage here. My name is Vikram Purohit and I'm one of the biotech analysts at Morgan Stanley Research. Before we get started, let me just read a brief disclosure. So for important disclosures, please see the Morgan Stanley research disclosure website at www.Morganstanley.com/researchdisclosures. And if you have any questions, please reach out to your Morgan Stanley sales representative. So, Chris, thanks again for joining us really appreciate it. Yeah, so I was thinking before we discuss any sort of pipeline specifics, if you could just give us kind of a quick overview of the business, the core thesis for why you created the company and kind of the current snapshot of the pipeline, that'd be a great place to start.

C **Chris Gibson** 00:58

Perfect, happy to do that. So Recursion was really founded with a central thesis that's probably not super controversial. And that's that biology is extraordinarily complex and when you layer on top of that chemistry, there's just this incredible sort of multiplicity of complications. And the reality is despite incredible scientists all around the world, dedicating their careers to trying to discover new medicines, the tools we have at our disposal, at least until recently have been overly reductionist. And so we started Recursion to try and leverage new tools, new techniques, new processes and a new mindset to really build a digitally-native biopharma company from the ground up and I think over the last nearly a decade, what we focused on in Recursion is building very, very complex high dimensional datasets of biology and chemistry at scale. So we basically have a factory full of robots that are churning out up to 2.2 million experiments a week across dozens of different human cellular types. And we turn those data into -omics data that we read out into an aggregating dataset. So we now have 16 petabytes of data growing over time, as opposed to the traditional approach where scientists do very focused experiments on a specific disease and then they move on to a new disease and there's not a lot of relatability of that data. We're trying to make one dataset that grows over time so we can start to see connections between data that we generate this week, and data we generated two years ago. And from those we're hoping to be able to identify completely novel targets. And I think

what we've built in Recursion, more than many of our peers and competitors I would say, is biology first. So we are not chemistry-first. There are some other companies, some of them here who I think have built incredible digital chemistry systems. The tools are much better than the ones that we've built today in that space. We really focused on understanding what is the target that we need to take into this particular disease and we want to have the courage to take that target forward even when it's not one that maybe is in the literature, or one that is maybe even challenging dogma. And that's been our approach so far. So the company was founded in 2013. We announced this morning two additional clinical starts, so three programs in phase 2 or phase 2/3 and a first NCE that we built in-house started in phase 1 this morning, and then a couple dozen programs coming behind those. Large partnerships in intractable therapeutic areas like neuroscience with Roche and Genentech, and fibrosis with Bayer that are helping us leverage all this technology, this Recursion Operating System we built into a variety of different therapeutic areas with our partners, and then building our own pipeline in genetic diseases and oncology.

V Vikram Purohit 03:45

Great. So building on that. Can you talk a little bit about the specific platforms and capabilities you've built at this point from an economic perspective?

C Chris Gibson 03:53

Yeah, so we have this central thesis at Recursion that in biology structure suits function, and so at the base layer of our operating system is an image based omics. Essentially, we use microscopes to take pictures of human cells, where we've broken different genes- every gene in the genome. We've added hundreds of thousands of different molecules or combinations of those things. And this is a new kind of omics called phenomics, and that's the foundational layer. We've done about 150 million experiments there, across every gene in the genome and multiple human cell types and hundreds of thousands of molecules. Beyond that, we started to scale things like transcriptomics. So we can do about 13,000 near whole exomes a week at Recursion, creating an orthogonal validation layer for image based insights. And then we also have started building other technologies and other steps of the process. For example, in translation, we put cameras in the cages of all of our animal models. And we can start to do more sophisticated readouts in our translational animal models. So we can see signals of efficacy that are typically unobservable using traditional approaches like the rotarod but also in our PK studies, we can identify tox signals early and actually raise flags on programs to avoid going down the wrong avenue much earlier. So you all are aware, a lot of times when people do these big case studies, they look at things like weight loss and death as the primary readout. It turns out that you can see vast changes in animal behavior and physiology using this machine learning approaches that are not correlated with weight loss or death, but are probably big flags. And so we're able to do that broadly across many of our of our programs at once. And we've killed a number of programs months earlier than I think we otherwise would have. What we're really trying to build is not a point solution for target discovery or hit discovery or lead optimization. It's trying to build a suite of tools, many in house but some partnered, we use tools like SchrÃ¶dinger's system, to enable us to use technology to remove bias. Use biology as a system - understand biological system across every step of discovery and development.

V Vikram Purohit 05:56

Great. You touched on that on the topic of competition and not competition other companies in the space. I think one topic that often comes up when people discuss this area is whether these different players are truly competing with each other in their one pilot. They're all going after these complementary efforts. What's your take on that?

C Chris Gibson 06:15

Yeah, I mean, there's a lot of disease in the world. So I think there's a lot of opportunity for companies to be successful today, despite incredible scientists working for decades, on average, about 90% of programs that go to the clinic fail. So I'll be happy if any company is successful on any trial, and I think all of us should be. So we're rooting all of our competitors and colleagues on. I do think that in the space of tech-bio, there's maybe a sense that there's competition, but again, the reality is there's so much disease to go after. I think it's really more about who's going to be able to demonstrate proofs-of-concept that continue to move the rest of the industry in this direction. And we feel that we're among the leaders in the field that are helping companies like for Genentech, for example, take on these more progressive opportunities to understand understand disease more more broadly. That feels good, but we're rooting our colleagues on.

V Vikram Purohit 07:08

Great. So on the topic of proof of concept, what are some of the early markers you've seen - efficiency, or R&D productivity, or quality of molecule - that's given you a good feeling that things are kind of progressing in the right direction for Recursion?

C Chris Gibson 07:24

Yeah, so we published some statistics in our S1 across about 100 programs that we've driven at Recursion, many of which we actually killed or terminated, which is an important part of the process. We don't have enough, you know, flux through our pipeline yet to get clinical data, but at least to IND what we were able to show is that we could go about twice as fast and spend about 80% less per program cost. There's often a fair criticism that we spent a lot of money, we raised a lot of money. A lot of that is spent on building out the operating system that we can deploy against many different molecules, many different programs, both our own and our partner programs. But on a per program basis, as this operating system gets better and better, we expect those numbers to continue to decline over time. And so, you know, one of the things that I think about is if you could imagine a company that could get drugs into the clinic, twice as fast for 80% less cost and meet the current probabilities of success, I think it'd be a successful company. I mean, if you can just get drugs to be clinically efficacious, I think you can build a pretty compelling company, but the real lever on the space will be improved probability of success. That's sort of the 10x shift in our industry is going to be to improve the probability of success at phase 2, phase 3. And ultimately, we need to prove that to the world with our current programs. But we also are building a system that's designed to get better over time. So our successes and our failures at every stage of the process inform the algorithmic approach to each of those stages. And so as we start to have scale, it's a really important piece of our design. We often get asked, what's your lead program? And we say, we don't have one. We

have a lead pipeline. And that's critical to the design of a machine learning system is that you need to create this sort of iterative cycle and learning because often the algorithm in the very beginning isn't very good. We've taken all of our drugs through the same translational models that any company would use so we have a strong sense that we'll be at least as good as the industry average, because we go through the same translational animal models, etc. But ultimately, we want to build an operating system that over time gets better and better.

V Vikram Purohit 09:28

Got it. And you alluded to this earlier, but just to put a finer point on it, what are the raw inputs that are feeding your different algorithms right now?

C Chris Gibson 09:35

So one of the things that's a little bit different about Recursion than many other companies is that most of our data that we use in our system is generated in-house. So we still use external data and there's value to that. But I'm reminded of a PI came to Utah when I was a PhD student from Boston and he brought an animal model with him and it didn't work. And after two and a half years, they finally figured out it was a change in the barometric pressure, or some of the altitude ended up being the issue. Biology is really complex. And it turns out that it's very hard to generate data across many different sites that's relatable. People just don't record enough. And so we took the expensive but I think critical decision that if you're going to build this technology, you have to control the data. And so we generate virtually all the data for our algorithms in house at Recursion. The foundational dataset as I mentioned earlier, are these microscopy images. We've got billions of those now for those who are ML and AI aficionados, they're perfectly labeled, which is important because we know what every robot did to every cell. So it's not like sort of the issue where you send autonomous vehicles out and they take pictures of everything and it doesn't know a stop sign from a traffic cone from a person and people have to label those things. We know what every image is because we constructed the data in that image. So I think that's an important point. On top of that, sequencing data. Proteomics data is something we're very interested in have done a little bit of work in, and then lots of bespoke assays to help us validate in patients, cellular systems, organoid models, etc. that the early exciting novel biology we found in our primary OS is validating across this later stage for translational work.

V Vikram Purohit 11:18

Got it. Got it. Okay. That's very helpful. Let me ask you one more platform question and then we should talk a little bit about some of your pipeline programs. I mean, looking 5-10 years out, if things progress the way you'd expect them to progress, and if positive momentum builds for for some of your pipeline, where do you expect the value proposition for Recursion to be rooted? Is it more in speed? Is it more in developing molecules for existing targets? Better isn't more for drugging currently undruggable targets and finding novel diseases that don't have any treatments? What do you think? Will you hope to fall across those different pillars of newer age medicines?

C Chris Gibson 11:57

Yeah, so I think the most important point is going to be increasing the probability of success. And I don't think it matters if that's a new target or an old target, a new chemical entity or a known chemical entity, a biologic or a small molecule. What matters is that we get medicines that work. And so that's where we want to ultimately see over 5-10 years the sort of rubber meets the road. That is by far the biggest lever any of us can pull is reducing that failure rate is at phase 2. So that's the critical area. But part of the way we get there is by developing a system that can explore more biology more quickly at less cost, because ultimately, that's how we start to get the reps into the algorithm to make it better and better over time.

V Vikram Purohit 12:37

Got it. Okay, fair enough. Let's transition over to the pipeline. First, you have a pipeline that's kind of diverse across therapeutic areas across indications. How do you prioritize what to go after and what makes sense?

C Chris Gibson 12:56

So we like areas of biology where there's large unmet needs, and there's some incontrovertibly known anchor points that we can sort of look in our maps at, but where there's really not a clear understanding of the downstream biology. So I think CCM, our first program, is a great example. This is a huge genetic disease. It affects about six times as many people as cystic fibrosis. Thanks to the genomic revolution, we understand that there are mutations in one of three genes aptly named CCM1, CCM2 and CCM3 that cause this disease with extraordinarily high penetrance. And other than that, we don't know a lot. There's lots of academic literature - Recursion got its start in the work I was doing in the lab of Dean Li, trying to build on that literature set and ultimately being wrong. We thought we'd identified activation of RhoA as the primary driver of the pathophysiology of this disease, built an animal model to prove that to ourselves, inhibited RhoA, and we made the animals worse. So that was this completely baffling experience where you're humbled in the face of biology where you felt like you had such strong evidence to suggest it this particular pathway was driving the disease. And maybe we had drugged out there's lots of explanations of why it could have gone wrong. But we were very, very wrong. And I think that was the moment where Recursion was was born. And we liked diseases like CCM, huge unmet needs, there's no other company going after the disease in the clinic that we're aware of. At least no companies have publicly stated they are in the clinic, a few academic investigator-initiated studies. And we identified a molecule that suggested to us a piece of the biology that we had underappreciated, and that was that you have this massive dysregulation of superoxide dismutase 2 in the endothelium. This is an endothelial autonomous disease, you can get the disease simply from having mutations in the cells that line your blood vessels. And when that happens, you get a huge accumulation of superoxide, and in the endothelium superoxide leads to all kinds of activating action. So you end up getting a breakdown in the cell-cell junctions, you get all kinds of dysfunction of the of the cell monolayer, and ultimately in the brain where this happens, it's an immune privileged organism, you start to get leak. You basically get this feed forward inflammatory milieu that drives the disease. And it turns out patients tend to have more symptoms when they have some other infection like the flu or something like that. So it all kind of makes sense. We totally underappreciated this. There was one paper from an Italian lab that had suggested that this superoxide mechanism was important, but the field had largely dismissed it. And then this

unbiased early approach we built - it was not really machine learning, it was sort of computer vision back in my dissertation - told us that the potential molecule to treat this disease might actually go after that particular target. And I think that was, that's a definition of the kind of disease we'd like to go after. We need some known anchor point of biology like genetic cause, and the rest of the biology is poorly understood. Got it, okay. Just walk us through the design of the study then, and where you've gotten so far over the next year. So because this is the first time a company had gone into the clinic for this particular disease, and it's a big disease, we've designed a phase two exploratory efficacy study in conjunction with our colleagues at the FDA. The primary endpoint here is safety and tolerability, because in these patients, there's really no treatment outside of neurosurgery. And certainly, if you have a single lesion on the periphery of your brain, that's a reasonable treatment. But a lot of the patients, especially patients with a familial form of the disease, will have dozens or hundreds of these lesions throughout their brain. And so this will be the first medical treatment if it were to be approved. And so what we're really going for here is trying to understand the safety and tolerability of this molecule because patients could take it chronically, maybe for life if it is efficacious. So that's the first sort of primary focus. Secondarily, we're trying to identify the right endpoint for a phase 3. And so we've got MRI outcome - that's one of the secondary endpoints, a couple of broad neurologic assessment tools that have been used and feel like we think that's important because the symptomatology of this disease depends on where the lesion is located. So it's a little bit challenging. Some patients have seizures, some have stroke. Some patients have focal neurologic deficits. And then the final endpoint is actually a patient reported outcome tool that we're building in conjunction with the University of Rochester. We enrolled over 600 patients in in the building of that particular tool, and we are reporting out soon at the Angioma Alliance, the patient group, the outcome of that patient reported outcome tool. It is a group that has built tools that have been used as endpoints with the FDA rare disease before. And so we're actually pretty excited about that particular tool. That'll be one of the four secondary endpoints.

V Vikram Purohit 17:55

What level of regulatory feedback or engagement Have you had on this program so far?

C Chris Gibson 17:59

We've had great feedback. We have Orphan Drug designation from FDA, we've had a lot of great dialogue with our partners that are not only on this indication, but actually all of our indications. And, you know, as new to the field, I was surprised by how collegial and sort of patient-centric our colleagues at FDA, where I think a lot of our colleagues, they're gonna get a bad rap, but at least in the context of smaller companies like ours, it's been incredible. They've helped us improve our studies. They've partnered with us to think about what will happen next. In the context of CCM, it's very clearly a phase 2 and phase 3. In our NF2 study, it's an adaptive phase 2/3. In our FAP study that we launched this morning, it's a phase 2, but there's the potential perhaps for this to be registrational study if the efficacy signal was very strong. And so yeah, we found them to be incredibly both our FDA and EMA colleagues to be really, really collegial. Have you provided any guidance on timelines to data for CCM? No.

V Vikram Purohit 18:59

Okay, got it. Maybe we can switch over to REC-2282, NF2, to give us a quick overview of where

that program currently stands and what some of the next steps are there?

C Chris Gibson 19:11

Yeah, so 2282 is an interesting program. We identified this in the context of a model of NF2 loss of function. What we identified on our platform may not sound surprising. We identified one class of molecules that modulates a variety of sort of oncology targets as HDAC inhibitors. But we got a really, really strong effective HDAC inhibitors and not other sort of classical oncology targeting molecules. So we expanded that initial dataset and identified a CNS penetrant, orally bioavailable molecule that had been in the clinic, but was abandoned. It was one of sort of three or four programs and a company's primary program read out negatively. And so it was bought back by the academic group at Ohio State and developed it, we licensed that molecule and now are in a phase 2/3 adaptive trial. In the context of neurofibromatosis type two we're going after meningiomas driven by mutations in NF2, as opposed to the acoustic schwannomas that are typically sort of pathognomonic for that disease. And that's because those acoustic schwannomas are encased in bone and it's really hard to have a strong image based readout for those to measure tumor volume. The meningiomas are much easier to measure. And what's interesting is beyond the genetic syndrome of neurofibromatosis type 2 sporadic meningiomas are driven by mutations in the NF2 tumor, a large proportion of the time so we can actually look at a slightly broader subset of patients in this particular trial. We're looking essentially at the reduction in the number of size of these lesions in patients over time. So it's a pretty straightforward endpoint. Got it. I guess fast forward to the time point where we have initial data from both of these programs, assuming they're positive components of the platform, do you think that would have helped to de-risk and what do you think was still be an open question even after that type point? Yeah, that's a great question. So most of the programs that are in the clinic now, we developed with an early form of the operating system, sort of circa 2018-2019. And so I think we will de-risk sort of the target discovery stage, ie hit discovery stage of the platform. There are programs now especially in the context of oncology, where we're using a lot more of the tools, digital chemistry tools that we both use from partners and ones we've built internally. Predictive ADMET tools, translational tools, like the animal model system I was talking about before. And so as you see our oncology programs move into the clinic, sort of target gamma, alpha, some of these programs that are in our late stage of preclinical work now, I think you'll find that those will be the programs that really start to de-risk our whole OS sort of from soup to nuts, but I don't think this is a static thing, right? And OS is designed to get better over time. And so this is going to be you know, our work over the next several decades is to continually refine the operating system. And there's interesting investments we're making today. I think one of the most important investments we're making is in the space of automated microsynthesis. Where today when we identify an interesting chemical series, our chemists often have to wait 8 to 12 weeks for molecules to be synthesized and to go through the next cycle. Using our platform, we see the opportunity if one could scale synthesis of many diverse small molecules in very, very small quantities to shrink that sort of 8-12 week cycle down to one or two weeks. And if you could do that, it means every one of our programs that could go onto this platform would go from sort of a 1-2 year lead optimization stage down to something that's much much more rapid. And so we see that as an important element of compressing the timeline. But what's more, automated microsynthesis also sets us up for what we'll call sort of autonomous search. So today, we've got hundreds of thousands of molecules physically in house at Recursion ourselves plus hundreds of thousands of molecules from our partners' libraries at Bayer and Roche-Genentech. And that's just a drop in the bucket in the space of small molecule, potential small molecule space. And so what we see is really exciting about

combining automated microsynthesis with our sort of functional biology tools and our digital chemistry tools is the opportunity to start building into chemical space and evaluating really, really rapidly so that we can autonomously search for novel chemistry that has completely new functions that you don't see with any of the molecules that one can access today.

V Vikram Purohit 23:37

Got it. Okay. Another important consideration for many investors is the topic of read through. What would you say about read through from one data readout within your own pipeline to another and then also data readouts from other players in the AI enabled tech development? Of biotechs development space?

C Chris Gibson 23:58

Yes, it's a great question. There's a number of companies that are sort of lumped into this tech biotech space. If you get really deep on all of them, they're pretty different. And so I think the reality is, is there's probably not a lot of read through between most of these different companies. But I think the perception that there's a very strong correlation between these companies, at least among the majority of folks in the market, so as we see early programs from companies like ours, Realy, SchrÃ¶dinger, Exscientia, all in the clinic at various stages, you know, I think that there's going to be some correlation as folks watch those early readouts. In terms of the pure tech bio companies that are building from the ground up, kind of across the spectrum, especially with a focus on the biology side or the chemistry, I think we're probably the one that's gonna create a lot of the early read through for others in that particular space and most of those other companies tend to be private at this stage.

V Vikram Purohit 24:58

Got it. Got it. So besides CCM and NF2, what are some of the early additional pipeline programs that have generated some excitement internally Recursion?

C Chris Gibson 25:08

Yeah, so obviously FAP - it started this morning, but I think some of the late stage preclinical oncology programs are what have me excited. One of my favorite programs is one we're calling Target Gamma. And in this context, our team looked at our map of biology - so we've mapped every gene in the genome and multiple human cell types, hundreds of thousands of molecules, and we can understand relationships between them in sort of a biological system. And there was a set of folks on the team who were interested in the target CDK12 in the context of HRT-negative PARP inhibitor resistant ovarian cancer. Very high unmet need, really critical space, because well, there's a lot of important validation behind it, but it's a very challenging target, both from a specificity perspective, but also potentially because of some on-target toxicity. And so when we looked in our map, we identified a gene that we're just calling Target Gamma, which heretofore has not been published in the literature to have anything to do with CDK12 biology, that has been published in other areas of biology, but really not known to be associated with the biology of this space. We also identified a molecule that we thought was

inhibiting the protein product of that gene, we biochemically validated that this is indeed an inhibitor of Target Gamma, and has no biochemical interaction with CDK12. That's clearly a novel target in the space. We went right into a PDX mouse model with an HRT-negative PARP inhibitor resistant tumor, and had 100% complete response in monotherapy. Within a few weeks on this novel target, we're really excited about the potential of our platform to identify these kinds of opportunities, where there's really no one that we're aware of going after this target or target class in the context of ovarian cancer. There's another great program Target Alpha in immune therapy, where we actually have identified using our platform, two targets that are required, they're sort of aesthetic for the response that we're seeing, very difficult thing to pick up from a biochemical perspective using traditional tools. But using our platform, we identified this molecule that seems to require inhibition of two different targets. And so that's another one to watch as we move towards the clinic as well.

V Vikram Purohit 27:24

Great. Maybe we could talk a bit about partnerships. So you mentioned what you have going on right now with Bayer and Roche. Are there other parts of the pipeline, or components of your different programs that you think would be amenable to partnerships? And if so, what would you be looking for in potential additional future partnerships, both from like an economic standpoint, and also from like a perspective standpoint?

C Chris Gibson 27:45

Yeah, so we really like to keep our internal pipeline focused on genetic disease, monogenic loss of function disease, really is the focus and then also on oncology, where you won't be surprised to hear we're mostly focused on genetically driven tumors. So outside of that context, we're pretty open to partnership and after our Roche Genentech partnership last fall, I would say that was you know, that was an important indicator for the field. It's not only the largest discovery collaboration in the tech bio field, it's actually the largest discovery collaboration from a total biobucks perspective that we're aware of in biopharma today. And so I think that got a lot of traction among, you know, BD and scientific teams across the industry. And we're always happy to talk to our colleagues about ways we can deploy our technology to help in the search that they have, and we know that our team can learn. We can't do all of biology ourselves as a small company today. So with each of these partnerships, we position ourselves to learn alongside and from sort of industry leaders like Roche Genentech, like they're in their respective fields, so that our team can be really, really good. So that one day as we pursue some of these broader indications ourselves will be very well positioned. So yeah, I think you can see us look to additional partnerships in the future, but they're going to have to be runway extending I think, you know, we've proven ourselves to the point now, especially in the capital markets environment we're in today, where I think we're probably not going to eat a lot of upfront costs, like we may have on our original Bayer deal.

V Vikram Purohit 29:16

Got it. Final questions to close out. Looking ahead 12-18 months, what are some of the key milestones people can keep in mind?

C Chris Gibson 29:22

So I think you can watch for us to continue executing on our current clinical program. Perhaps to give guidance on readouts for some of those. You should see us put more programs into the clinic or have additional INDs, you may see us have options from our partners. Either program or map building options. And there's a potential for, you know, another large partnership. I think those would be the core things to watch over the next 12-18 months.

V Vikram Purohit 29:48

Great. With that we're out of time. Chris, thanks so much for joining us. Appreciate it.