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<<Gil Blum, Analyst, Needham & Company>>

Good afternoon, everyone. My name is Gil Blum, and I am a Senior Biotech Analyst here at Needham & Company. It is my pleasure to have with me today Recursion CEO, Chris Gibson. So as a reminder everyone, any viewers who are watching through our conference portal are able to submit questions via the ask a question box below the video feed and window.

And with all that, Chris, I think maybe a bit of an introduction, so Recursion is a new breed of company in biotech. Could you maybe walk us through the reasons for forming the company and maybe what is the main problem that you're strategically trying to solve here?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Yeah, happy to, Gil, and thanks again for hosting. Excited to be here. Recursion was actually founded out of work that I was doing in my dissertation with a guy named Dean Li. And some of the investors may know Dean is the President of Merck Research Labs. We were working together at the University of Utah, and we were trying to take a traditional approach using molecular biology, cellular biology tools to advance a potential medicine for a rare genetic disease that was poorly understood.

And after over a decade of work in Dean's lab and my contributions for a couple of years, we ultimately tested our hypothesis and failed. And I think this is not surprising. 90% of drugs that go into the clinic fail, and the vast majority of those drugs fail due to a lack of efficacy or some surprising, unexpected sort of systemic effects on sort of toxicity.

And I think the reason that we still have such a high failure rate is that biology and chemistry are massively complex. And at the end of the day, hundreds of thousands of scientists are doing their very best work, but operating against a system as complex as biology, it's very challenging.

And Recursion was founded out of a belief that there was a rise in a number of tools and in particular technology tools that could allow us to actually build pretty sophisticated models of really, really complex stuff. And I think what's on everybody's mind right now or at least many people's mind is ChatGPT a very sophisticated model of language that's allowing us to understand huge swaths of data, everything on the Internet, all in one place, and interact in a pretty compelling/creepy and scary way with all of us as humans.

Those same sorts of tools, AI, we believe can be deployed to biology to help dissect really something too complex I think for humans to understand. We can understand parts of it, but not all of it as a single system. And that's what we're doing at Recursion. And I think what's very different about us than almost every other TechBio company, because when we've started, there were maybe 10 companies in this space back in 2013, there's now hundreds. We are very

focused on biology, not just chemistry because we think understanding the right target is more important than a better chemistry tool, although the both of those are important, but we're also focused Gil on building both the computational tools, but also the wet lab tools. We believe you have to have the right data.

And so we've been working to build a massive factory full of robots that puts out data on nearly 2 million experiments every week. And today, we've generated 21 petabytes of proprietary data. And just like OpenAI trained ChatGPT on the Internet where most of that data is free, Recursion is now in a position to train sophisticated neural networks across a completely proprietary data set. And unlike the Internet, we don't believe that the same data set exists freely available for the biopharma industry to use to leverage these tools. And so we've been working really hard to build that.

<<Gil Blum, Analyst, Needham & Company>>

Well, as a recovering scientist, I totally find this very appealing especially the 90% failure rate, which we're all very familiar with. Maybe to walk a little more through the features of the Recursion OS, I mean, would you say the key differentiator here is effective? It is a proprietary database that is generative meaning you run your own experiments.

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

That's right. And we run them at massive scale. In fact, we just put out a paper over the weekend, a preprint where in bio archives where we show a really interesting potentially detrimental feature of Cas9 nuclease activity, a causing chromosome arm scale truncations. And we are only able to show that because we've knocked out every gene in the human genome with five or six different CRISPR guides in multiple human cell types.

That is a very difficult thing to do. In fact, it's been done by very few labs on earth. But Recursion not only building all this technology data, we're operating one of the most prolific data generation engines in all of biopharma. And so we're very excited to be not only leading the technology revolution of this industry, but operating at massive, massive scale on par with many of the largest companies in the space in our own data generation and that is absolutely, I would say, the core competitive moat that we've built.

You can't train an amazing neural net without the right training set. And Recursion has built what we believe is the most compelling training set in all of biology, and we think we're several years ahead of anyone else building something similar.

<<Gil Blum, Analyst, Needham & Company>>

When you're reviewing a novel assay or capability, what kind of decision making process goes into whether you should include in an operating system or not?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

So lots of – lots goes into these decisions, but what we generally look for are data sets that can be generated with high quality at scale for relatively low cost that give a tremendous amount of useful data and that seems kind of like an obvious statement, but it turns out when you evaluate many assays, you can do lots of assays at high scale for very little money like a plate reader assay, but you can only read out one thing at a time like does this protein go up or down? Is it phosphorylated more or less?

At Recursion, we like to read out very rich complex datasets like omics data. And when you look at the space of omics, transcriptomics, proteomics, metabolomics, there really is not an assay that we felt like could scale to sort of millions of experiments a week until the new kind of omics that we helped pioneer based on work of a woman named Anne Carpenter at the Broad Institute called phenomics.

And this is actually taking microscopy images of human cells and using computer vision and neural networks to extract cell morphology, a lot like a pathologist who looks at slides can diagnose hundreds of different oncology diseases and other kinds of diseases through looking at images of your cells on a slide. We're training neural networks to look at images of cells in the lab and to turn those into mathematical representations of biology.

When you do this at scale, you can start to see all kinds of really interesting relationships. And so that's our foundational layer is images of cells we call it phenomics. That's what our paper we just put out kind of highlights, but we've also started scaling transcriptomics, at Recursion, we can do 15,000 exomes a week. We're exploring things like proteomics and other tools and we've actually integrated something we call in InVivomics another new kind of omics skill, where we take cameras in the cages of all of our animals, we have our own vivarium, and for translating our molecules more quickly with fewer animals, we actually use computer vision and machine learning to extract signals of essentially animal behavior.

So is the animal breathing more or less? Is it acting moving more or less? Is it – it is its furl look matted? All of this is automatically computed to identify not only whether a drug might be doing what we want, using a more robust approach than traditional animal assays, but also giving us a lot of insights into potential toxicities.

So we can recognize things like liver tox or kidney tox or heart tox simply from a video of an animal in a cage. And this is helping us really accelerate the translation process as well. So you can think of Recursion as an integrated company building technological solutions across large rich datasets that we build in-house that, that address many steps of the process of discovering of a medicine. It's really a full stack operating system that we've built.

<<Gil Blum, Analyst, Needham & Company>>

Okay. And given the level of investment you're describing here, what proportion of your spend would you say you invest every year and expansion of the capabilities of the platform versus let's say clinical development?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

So we have five programs in clinical development now, three programs in Phase 2 or Phase 2/3 studies. Another program headed into Phase 2 and one in Phase 1. But we really focused those in I would say precision or niche areas of biology, rare disease, for example. And so those trials actually despite the fact that we're operating with five clinical programs, those trials represent a minority of Recursion spend.

I would say, the majority of our spend is on supporting this platform, which underlies new programs at Recursion, but also with partners. And we have significant partnerships including a large neuroscience partnership with Roche Genentech, which we'll happily talk about a bit later, I'm sure.

In terms of our actual investment in expanding the platform into new areas, I would say it's probably on the order of 10% or 15%, Gil, a lot of the expenses in running the operating system we've built to turn out what we hope will be dozens of new exciting programs next year, as well as dozens of new programs for our partners as well. And then the clinical programs are a minority, I think probably on the order of about 20%, 25% of our spend.

<<Gil Blum, Analyst, Needham & Company>>

Okay. And before I move on to discussing the collaborations, I know we touched on this a little bit, but maybe a little more on the moat that you're creating from competition. I mean, it's a little hard to have clear insights as to what large biotech is doing, or large pharma for that matter, but your own gut feeling, do you think that there's some secret, super secret development going on there? Or what do you know given all the experts in the field these days?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Well, certainly, when we started back in 2013, the idea of using machine learning in drug discovery and development was, I would say completely ignored by most and laughable to many. Today, it's very different. Every major pharma company has I think a legitimate effort focused on trying to leverage machine learning in some way shape or form.

And certainly, our partners at Roche Genentech at Bayer are really advanced in those ways. Yeah, I think Janssen with Najat Khan also leading the way. But a lot of these groups are, they've got to build machine learning into commercialization, clinical development, discovery, et cetera. And because they also have so many other priorities working on different modalities, all of their commercial programs, et cetera, I think Recursion really is leading the way. There's no way to tell for sure, but there are indicators that suggest that we are leading the way.

I think a good example is there's a dataset that was put out earlier this year called JUMP-CP actually driven by Anne Carpenter, who's one of our collaborators and the Broad Institute. And there were a number of very large pharma companies, several of them who were part of this pre-competitive consortium to build a dataset that they could share with the world.

And we're so glad they did. It's a really compelling dataset. But it represents about one week's worth of Recursion's data generation. And so while it's exciting to see this field moving in this direction, we really do feel like we have multiple orders of magnitude more data generation. And I think if you actually look at the preprint we put out this weekend, our data seems to be able to recapitulate known biology better than some of these other datasets. We're working in primary human cells in many cases as opposed to cell lines.

We have many higher replicate numbers. We have a lot I think more sophisticated computational tools in the background. So we're able to pull out more interesting rediscovery of known biology at a higher level than some of these other datasets. And we think that sets us up then to have higher confidence to go after the novel biology that we and our partners get really excited about.

<<Gil Blum, Analyst, Needham & Company>>

Yeah. That's the great analogy set a moment for ChatGPT, a program that knows 50 languages without being taught 50 languages. So the cool aspect is if you have a large enough database, there are basic connections that machine learning can make that human cannot. And then I think that's a really exciting proposition per machine learning.

So let's talk a little bit about collaboration. In our own way of looking at Recursion, we consider current and future strategic partnerships to be pretty much the primary value driver. So maybe to set the stage, can you remind our audience about your existing deals with Bayer and Roche and maybe a little bit the structure there?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Sure. So the first significant partnership, we signed was with Bayer in fibrosis. That deal was signed in the fall of 2020, so we're coming up on 2.5 years in. And actually the subsequent year, in the fall of 2021, we significantly expanded that collaboration to use our newest set of technology that we call inferential search. It's a more powerful approach.

We're very excited about the field of fibrosis at Recursion. We see a lot of I would say, accelerated interest in the space. And so as we continue to develop programs, we can't share a lot about them, but as we continue to develop programs up to meaningful inflection points with our partners at Bayer, we're very excited about the opportunity to drive those programs forward for patients and hope to be able to share more in the near-term.

We signed in the fall of 2021, just over a year ago now, right at the end of the year, a really substantial partnership with Roche Genentech. It was one of the largest discovery collaborations in biopharma history with over $150 million upfront up to or exceeding $0.5 billion in milestones related to building datasets and sharing those datasets with our colleagues at Roche Genentech.

And then up to $300 million per program for up to or exceeding 40 programs really focused in neuroscience and a single oncology indication and it's a decade long collaboration, really exciting, because Genentech is now led by Aviv Regev from a research perspective. Aviv Regev

being the first computational biologist, actually from the Broad Institute as well, to now lead a major research group, major research entity in biopharma. So very excited to be kind of the foundational partnership with her and her team to go after neuroscience, an area where we know there's been a lot of challenges.

So substantial deals certainly when we think about how to partner at Recursion, what we look for are industry-leading partners who are interested in novel targets and novel target disease relationships, because that's I think where Recursion really excels. And I would also say companies that are willing to put the resources into complex intractable clinical development, at Recursion, we really want to focus on precision oncology and rare diseases for our own clinical development where we can run a Phase 2 trial for $10 million, $15 million, $20 million if we're going after fibrosis or big neuro diseases like Parkinson's or Alzheimer's or something like that. One can imagine these trials could be hundreds of millions of dollars in some cases.

And so we want to partner with the best to go after some of those big intractable areas. And that's why you see us partnering in areas like neuroscience. You could perhaps see us partnering in the future with other areas that we see on the rise. Good example would be cardiometabolic. That's an area we see as on the rise and also an area where the clinical trials are massive, really hard clinical trials.

And so we would want to leverage the expertise of a partner, but they could leverage the expertise of our platform and our team to find really interesting novel targets in that space. So that's really how we think about partnering.

<<Gil Blum, Analyst, Needham & Company>>

I know this might be an area that you may only allow enable limited disclosure, but we get asked about this all the time. Can you give any guidance of maybe when we could hear about new opt-ins or milestones in this calendar year, or whatever information you can give investors?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

The guidance we've given Gil is that we do think that there will be programs at an option stage in the near-term, and that there will be perhaps milestones related to our data generation and data sharing with Roche Genentech in the near-term. So we have given that guidance, certainly we have to continue performing well, but we think we're on track or ahead of schedule in various parts of our partnerships both with programs and the underlying data. So we're excited.

We will of course share as soon as we can, but we of course can't share before we meet those milestones and have clearance from our partners to do so. The other thing that we can talk about at some point is, we've traditionally talked about biopharma partnering and even in, after we announced the Roche Genentech deal, we said we're going to not try and sign any new partnerships in 2022 because we really need to deliver on this partnership.

We became just in 2022, we went from zero neural iPSC cells being generated at Recursion to half a trillion neural iPSC cells. And for folks who aren't aware of the scale of that industry, we

believe that makes us the world's number one producer of high quality neural iPSC cells in a single year. So when Recursion says it's going to go focus to deliver on something, I think we really do deliver well, now coming into 2023, we certainly are open to significant partnerships with biopharma, the right partnerships quality over quantity for us.

But we also gave some guidance in our 10-K that because we're seeing this incredible acceleration of AI and ML because Recursion has generated the dataset we see as most useful in the context of building some of these large models, that one could see us potentially also partner with large tech to accelerate our delivery of these technologies more broadly to more biopharma much like OpenAI did with Microsoft to accelerate that delivery as well. So certainly, exciting to be a company that could partner not only with large pharma, but potentially with large tech.

<<Gil Blum, Analyst, Needham & Company>>

Okay. And maybe kind of a last point here. So do you feel certain potential partners maybe hanging out on the sidelines waiting for a clinical proof of concept?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

I think lots of folks are waiting for clinical proof of concept from investors to certainly partners. And I think Recursion is really leading the tech biospace. There's a handful of other prominent exciting TechBio companies who have clinical stage assets, but I think Recursion is likely to really be the first to read out some significant efficacy endpoints. And so lots of people are waiting on that.

What I'd say though Gil is, while we are excited to give those readouts, I think there are a lot of leading indicators of success that one can look at. And these are the sorts of data that our partners like Roche Genentech got comfortable with to do such a large scale collaboration. And one could find themselves a bit behind the curve if you wait all the way until those readouts.

And I think a great example, this is in our corporate deck in the kind of app – in the appendix, but we generated a very, I would say, messy by our internal standards dataset in the first few weeks of the pandemic, published a preprint in mid-to-late April of 2020. So weeks into the pandemic, we got live SARS-CoV-2 virus at a BSL-3 facility and ran a small screen against just 1,700 FDA approved drugs or nearly FDA approved drugs.

And so far, nine of those drugs have ended up going through randomized controlled trials against SARS-CoV-2. The prediction we made in April of 2020 before any of those trials readout has been correct in terms of predicting the trial readout in humans in eight out of nine of those trials. So we predicted that hydroxychloroquine had no useful benefit in the context of SARS-CoV-2, before when this was still a real topic before there were many trials demonstrating that effect.

We predicted that remdesivir had a positive effect before that trial readout and you can go down the line. The only trial that we are aware of that we made a prediction on the molecule and got wrong was dexamethasone, which acts via a pretty complex kind of systemic effect. But other than that, eight out of nine of those programs we predicted correctly. Those are the kinds of

leading indicators that don't necessarily tell us that our trials will or won't readout positively, they're independent. But they certainly give us and our partners some belief that it is worth getting ahead of what we believe will be a revolution. And it's not just Recursion. There's many other really, really credible, competent companies in this space as well.

<<Gil Blum, Analyst, Needham & Company>>

I would say that maybe where investors have some challenges is when it comes to the fact that if you're searching for novel biology and novel agents, you're going to come off sometimes with things that are not obvious, right? That's sort of the whole idea of using the power of AI, right? Because otherwise, it was an obvious solution, you don't need AI for that.

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Well, that's right. And we know what the track record of – I'm not going to say obvious solutions, because there's some really non-obvious compelling different solutions too. But we know what we're capable of as an industry today and it meet and it's a 10% success rate through the clinic. And I think if you look at the way technology has shifted virtually every industry except for drug discovery and development, and it makes sense, very complex, highly regulated that this would come late. But we're starting to see that healthcare and drug discovery development biopharma are on the early end of the same kind of shift we've seen in almost every industry. And the question is, is there something about biopharma that's going to be fundamentally different than every other industry in the world? And I'm sure there are some very specific things, but ultimately I cannot imagine a future where the application of ML and AI is not an inevitable game changer for this industry.

So your question is, which is the company that's going to lead that revolution? I think Recursion has a lot of data to suggest that we may be one of those companies. We certainly have the largest clinical stage pipeline of any company in the space, the largest partnership of any company in the space. And I think one of the most sophisticated teams. And that's from our research associates all the way up to our board. And we think we're ready to deliver and very excited to share with the world as we hope and to share the outcome of these trials and many other new trials that we hope to be initiating as well.

<<Gil Blum, Analyst, Needham & Company>>

All right. So shifting gears can go a bit into the clinical programs themselves. So maybe starting with cerebral cavernous malformations. Just to remind our audience, not a lot of people know this indication or what is the epidemiology here standard of care?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Absolutely. Thanks. So this is – yeah, cerebral cavernous malformation or CCM for short. This is a very prevalent rare disease. I recognize I said that on purpose. But there's more than a million patients worldwide who have lesions associated with this disease. But a subset of those patients are symptomatic, about 360,000 patients in the U.S. and Europe. Patients get this disease

in one of two ways. Either they're born with one allele mutated in any one of CCM1, CCM2, or CCM3. And these patients who have a familial form of the disease get a loss of heterozygosity in many cells across the central nervous system. And essentially what these patients get, it's almost like a small aneurysm, Gil, but it's in the capillaries of the central nervous system.

And so what ends up happening is these lesions become leaky. And when you have leakiness of blood into the central nervous system, you get inflammation and hemosiderin because it's an immune privileged organ. And depending on where these lesions arise, these patients can get anything from focal neurologic deficits like blindness or headaches to epilepsy and then all the way across to hemorrhagic stroke.

So it's a very – it's almost like MS in the diversity of symptoms that the patients get. But what's exciting for patients and for us is that we are the first company to go to the FDA with any potential treatment for this disease. And we're not aware of any other company in the clinic or even in late preclinical studies. So we're – many years ahead, we believe of anyone else and we're hopeful based on our animal model and our human cellular data that we've identified a potential therapy here that has the potential to reduce the symptoms of this disease and perhaps slow its progression as well.

And we initiated a Phase 2 trial last year, just over a year ago actually, which is exciting because that's suggest that we've had patients now on drug for a year or more. And certainly in this disease, where the only treatment, the kind of standard of care is neurosurgery, which only works for patients who have lesions in a part of the brain that's accessible. And certainly is very challenging in patients who have the familial form of the disease, because they can have 50, a 100, a 1,000 of these lesions. So we're excited to potentially be in a position to provide the first molecule that could actually slow the disease and/or decrease the symptoms of the disease in this relatively large rare disease population.

<<Gil Blum, Analyst, Needham & Company>>

So if you had to hypothesize, what – why aren't people not familiar with this in investing community, for example?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

This is a great example of a classical undruggable disease. The three genes that we know cause this disease. We don't understand the downstream biology very well. They actually encode scaffolding proteins, which are classically not considered to be something you can drug. And we don't really know how disruption in these scaffolding proteins ends up resulting in this diverse symptomology of the disease. But this is exactly why we're so excited about Recursion's platform is because we can take an unbiased approach to take a known piece of biology. We know that a mutation in CCM1, CCM2, or CCM3 causes this disease.

And then we can look in a very unbiased way at thousands of potential mechanisms that could help restore function without having to understand all of the biology. And certainly since our

initial discovery, the understanding of the biology has gotten better, but not good enough for any other biopharma companies that we're aware of to actually advance the program into the clinic.

Our molecule actually targets superoxide, which we didn't really expect was an important part of this disease when we were first studying it. It turns out the molecule hitting that particular target and restoring many of the effects, the functions of human cells in which we modulated CCM or animals in which we modulated CCM genes actually told us something really important. It told us that maybe superoxide is important and we were able to trace that back up to some dislocations in FOXO1 transcription factor, we still don't totally understand how that is related to CCM mutations, but we've convinced ourselves that there's a specific effect to mop up superoxide in the endothelium that has a really important restorative function across multiple measures of vascular function in this disease. And that's exactly where our platform shines. We can go after diseases that traditional tools are not well placed to go after.

<<Gil Blum, Analyst, Needham & Company>>

Okay. Maybe a typical question for rare – sort of rare disease enrollment. Have there been challenges on getting your patients for your Phase 2? Are they patients easily identified and enrolled?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

So actually this particular Phase 2 is going really well and a lot of credit to the Angioma Alliance, which is the patient foundation that we work with here, that's really helping bring patients to these trials and some of the great investigators and their teams who've been working hard. So we're on track with enrollment for this particular program. And certainly any rare disease is harder than very large diseases. But we're right where we hope to be with this particular program and pushing very hard. There are other trials where enrollment has been as we've shared in the past, our FAP trial, we've had a harder time enrolling and made some protocol amendments to help reduce the investigator and patient load to increase the enrollment rate there.

<<Gil Blum, Analyst, Needham & Company>>

Okay. And jumping to a similar but slightly different indication NF2 meningiomas, can you give us again an idea of how many people are affected? This is a, I would say, pretty rare indication. And how is the study that you guys are currently conducting different from previous effort with a similar molecule?

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Yeah. Happy to share, Gil. So we identified this potential effect of a molecule in NF2 mutations. And NF2 mutations lead to really two different diseases. One is a syndrome called neurofibromatosis type 2. It's classically associated with deafness in one ear. People get these acoustic schwannomas, but these patients also get a number of other tumors including meningiomas in their brain, which can be very difficult to remove. There also are sporadic

meningiomas that are often driven by NF2, and we're going after both of those populations. We think that's about 33,000 treatable patients in the U.S. and Europe. And there are no approved drugs for NF2 or NF2-driven meningiomas, the standard of care really is surgery when possible.

So we're excited about the potential. This molecule has been tried in a number of solid tumors as part of Phase 0, kind of investigator initiated trials under a company called Arno Therapeutics before it went to funk when one of its more advanced programs failed many years ago. We identified the unexpected opportunity being really, really strong in NF2, but not in other kind of oncogene or tumor suppressor gene contexts as part of our platform that led us to in license this molecule which had some limited clinical data. We then filled that out and initiated this adaptive Phase 2/3 study that's really focused not on kind of lots of different kinds of solid tumors. It's focused on NF2 mutated tumors, which our platform told us was where we were going to see a lot of specificity with this particular molecule.

<<Gil Blum, Analyst, Needham & Company>>

So there is some data with NF2 mutations as well with REC-2282. And I mean, it would need to be stronger than what you've seen before in order to move forward. Maybe you could put that into context for us.

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Sure. There were a handful of patients, I think four patients who had NF2 tumors that were part of 40 or 50 patients that were part of these Phase 0 trials. We got two useful pieces of data there. A couple of these patients had their tumor resected well on drug. And so we were able to get intratumoral drug levels based on oral dosages that helped us tune based on what we've seen in our in vitro data that helped us tune the dosage levels that we are shooting for in our clinical trial. So that's one.

And two in a non-statistically significant way, some of these patients demonstrated trends towards a reduction in growth or actually a reversal of growth of these tumors. Now these are relatively slow growing tumors and there were only four patients or so. So we don't want to over-index on those data, but certainly some patients saw enough utility from this medicine that together with their clinician, they stayed on the drug for several years.

That tells us something about the safety, that a subset of patients were able to tolerate this medication for years. And it also tells us that at least some patients and their physicians believed that they were seeing a benefit that was worth exploring. Now, again, we are not relying on those data. They're insufficient to make any sort of statistical claim, but they certainly gave a trend in the direction and gave us some useful context for deciding on our clinical trial design. It's a relatively long trial. We believe based on the growth of these lesions that we need to treat for 26 months to actually demonstrate significant effects of reducing the growth rate or slowing the progression of these tumors.

And so that's why we've adapt – gone for this adaptive Phase 2/3 trial design where it's – with 20 patients have been on drug for six months as part of our Phase 2, we'll do an interim dose and

safety readout that'll help us make a decision and go to the FDA to begin potentially a Phase 3 trial in parallel. Certainly, we would not expect significant efficacy findings given the slow growth rate of these tumors at six months. But if we find anything unexpectedly exciting we will certainly let everyone know as well.

<<Gil Blum, Analyst, Needham & Company>>

Okay. Let's move on to another tumor causing syndrome. And this is FAP with the AXIN1 and APC mutations. So again, maybe short description of what this is and how common it is, especially, in colorectal cancer.

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Yeah, absolutely. So this is a disease where patients are born with mutations in a gene called APC, which is a widely known gene in oncology. And these patients end up getting hundreds of polyps in their colon, and if they're not treated they will end up 100% of these patients will go on to get colon cancer. Now, colon cancer can also arise out of sporadic mutations in APC. APC mutations account for a significant minority of general colon cancer. But in this trial, we're really focused on the familial genetic disease called familial adenomatous polyposis, where these people get these pre-cancerous lesions.

Now, the standard of care for these patients is pretty impactful. They actually have to have their colon removed in their late teens or early 20s in order to prevent colon cancer. Even after their colon is removed, many of these patients still end up getting colon cancer with lesions that developed at the end of the small bowel or in the anal pouch areas that are not removed as part of the colectomy.

And so we're looking in patients post colectomy. Can we reduce the burden either decrease the growth rate of new polyps or even reverse polyps, which is what we saw in our animal model. We almost completely eliminated all polyps in our animal model, including dysplastic polyps. And that's important because there is a clinical gold standard here. It's a bad one. But celecoxib is a drug that has been used in the past to treat these patients. It did slow the growth of new polyps, but it turned out it didn't really shift the incidence of cancer in these patients whereas what we saw in our animal model was that celecoxib did prevent the growth of new polyps, but it didn't reduce the number of polyps that were dysplastic.

Our molecule in a dose responsive manner not only prevented the growth of new polyps, it actually eliminated polyps that existed in the animal at the beginning of the trial and significantly reduced, almost completely eliminated dysplastic polyps. And those are the ones that people really care about.

So we're excited to see if we can replicate that data in humans. And certainly if we can, it could mean these patients have a lower oncology risk and it could set us up in the future to actually explore the potential to delay colectomy at this very sensitive age of the late teens to early 20s. But that's a trial that one can't do today without better evidence.

<<Gil Blum, Analyst, Needham & Company>>

So just talking here a little bit about a potential clinical program, do you think the company's planning to use similar endpoints to the one scene with other studies, two years polyp number and size progression to cancer? I mean, I'm just spitballing some potential endpoints here.

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Yeah, absolutely. So in this particular trial, what we're actually going after are primary endpoints related to the change from baseline in polyp number histological grade and disease scoring. And so this will be a six months of treatment study. So after we do kind of a dose run in PK run in then we'll – which we've already done, then we'll be in a position or we will be doing soon, then we'll be in a position to measure basically the change in polyps. So it's actually very much like the mini trial we did in mice from an endpoint perspective.

<<Gil Blum, Analyst, Needham & Company>>

Okay. Because we are running short on time, and I don't want to neglect to C. diff especially because this is a new chemical entity, which makes it particularly interesting. Maybe you can put in context unmet need in CDI.

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Yeah. So C. diff is a huge area of unmet need. The disease affects over 700,000 patients in the U.S. and Europe every year. And there are tens of thousands of patients that die of recurrent C. diff every year. In fact, probably some of the folks who are watching this now have actually experienced the disease. It's caused by a microbe that in the context of antibiotic treatment can grow kind of out of phase and end up taking over the gut and it releases a toxin that degrades the lining of your gut and then leads through this feed forward inflammatory milieu. Recursion actually used C. diff toxin in our assay to identify lots of molecules that could affect the toxin or the host targets. We identified several mechanisms and ended up advancing this particular molecule series through optimization and this is an antitoxin.

So this is a drug that doesn't target any host protein, so it's not actually affecting your own body by design, and it doesn't actually go after the microbe. So it's not antibiotics. So we don't believe resistance will be an issue. It's a drug that actually reduces the ability of the toxin itself to use its own enzyme that's encoded on the end that cleaves it and makes it active. And this is an area that's actually been validated clinically. So Merck has a drug called bezlotoxumab. It's an antibody that soaks up the toxin and has really nice efficacy. It turns out that sales were not as hoped a few hundred million dollars a year, because it's hard to get people to take an antibody, an expensive treatment in the context of a disease where vancomycin often works. Now the problem with vancomycin, Gil, as you know, is that it also causes the disease, it's an antibiotic.

And so it's kind of this chicken egg issue, I'm not convinced that we have a good treatment for this disease. And I think that an antitoxin that is a small molecule, inexpensive to manufacturer could be really nicely positioned if safety and efficacy are really robust. And we're doing the

Phase 1 trial now. We expect to read those out later this year. And we've had a lot of interest, I would say, from biopharma around the potential for actually licensing this asset to go after not only recurrent C. diff but perhaps a broader population if one could have a very safe and efficacious small molecule treatment. And that's exciting for us as our first new chemical entity to get this kind of interest. And I think that might be the right path for this molecule because from our side the kind of trial one would want to run ideally in Phase 2 in infectious disease is a pretty big trial and something we might like to partner with large pharma on.

<<Gil Blum, Analyst, Needham & Company>>

Okay. We are running up on time, and although I have many, many more items to discuss with you, Chris, I'm going to have to stop at this point. Again, thank you very much for attending our conference and taking the time.

<<Chris Gibson, Co-Founder and Chief Executive Officer>>

Absolutely. Thanks, Gil. Fantastic conference. Appreciate it.