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<<Yatin Suneja, Analyst, Guggenheim Securities>>

Okay. Welcome, everyone. My name is Yatin Suneja, one of the biotech analysts here at Guggenheim. Welcome to our inaugural Healthcare Innovation Conference. Our next presenting company is Climb Bio. From the company, we have three executives here, on my left here we have Aoife Brennan, President and CEO. We have Brett Kaplan right there sitting next to me as he is a COO. And we have Bill Bonificio, Interim Chief Business Officer.

Thank you for joining us. Aoife, I'll hand it over to you. Why don't you maybe give a five-minute overview of the company relatively young companies, just talk about the asset, what are some of the upcoming catalysts and then we'll go into sort of a Q&A.

<<Aoife Brennan, President and Chief Executive Officer>>

Great. Thanks so much for the opportunity. It's wonderful to be here. We were a relatively late addition to the roster here. We're a company that's just recently rebranded. We were previously known as Eliem Therapeutics. The company was originally a neuroscience company. And we recently acquired an asset that was in a private company called Tenet Medicines. Bill was actually a founder of Tenet Medicines and is here to provide some of the important background on our lead asset, which is budoprutug.

And the company was really kind of formed around the opportunity in B-cell mediated diseases. We believe based on some of the emerging data around CD19 in particular as an important target in B-cell mediated diseases, that there was an unique opportunity to pursue a naked antibody based approach to B-cell depletion. And we saw that there was a real space and a gap in the market, was a number of other modalities that were pursuing this space. We can get into a little bit later in Q&A some of the strengths and weaknesses of those other modalities. But there was this gap in terms of naked antibody based approach that we felt presented a real opportunity for a biotech company to pursue.

And we were lucky in that there was an available asset that had been substantially de-risked. It was an asset that already had a very nice clinical data set. It had been studied in oncology where it had been evaluated in a dose escalating study and also had an early data set in a interesting indication called membranous nephropathy and we can tell you a little bit more about that.

So an existing asset that was in the clinical stage in this really exciting indication in a kind of a white space area of naked antibody based approach to B-cell mediated diseases. And so the company came together with a lot of great investor support with this public company, Shell [ph] that existed for in the case of Eliem and this all happened at the beginning of the summer, I joined as CEO. We rebranded the company just in October and launched as Climb Bio. We're in a very fortunate position and that we have a very strong balance sheet.

We have ability to do additional BD in licensing and the focus of the company is really going to be around developing biologic therapies for I&I indications where we really feel we can develop transformative therapeutics for patients who have unmet medical need in the I&I space. And we believe that there are many interesting opportunities there that are kind of being overlooked by others. So very exciting space and looking forward to continuing to build the company as we go forward.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Very good. That's a good overview. Bill, why don't you maybe – I'll pick your brain on this. How is your asset differentiated relative to inebilizumab or some of the work that we are seeing with other players in the CD19 space?

<<William Bonificio, Interim Chief Business Officer>>

Yeah, I'm happy to opine on that. So as you all may know, there are a couple other anti-CD19 antibodies naked mAbs that are in development or approved, the most relevant of which is inebilizumab. It's an anti-CD19 antibody from Amgen, was originally developed by MedImmune and then went to ViaLase [ph] as you may be familiar with to Horizon and now to Amgen.

We like to use that as a comparative molecule. The other one tafasitamab is approved in oncology. We don't think it's going to go into autoimmune. But in terms of the differences between our drug budoprutug inebilizumab, there's a few important ones. First and foremost, we think on a per molar basis, we're a bit more potent than them, say 5 to 10 times more potent in terms of B-cell depletion assay. And that allows us actually to go to dose at lower doses and get to subcutaneous doses.

We think that subcutaneous administration will be important in autoimmune diseases as we've seen play out elsewhere, say in the MS market or the SLE market subcutaneous matters and we are bringing forward a subcutaneous formulation. It's worth noting that inebilizumab early on did try subcutaneous administration. They were unable to match the exposure profiles they were getting with IV and so they did not bring that forward into pivotal studies and it's unclear that they will ever be able to do that. And so we think that's one important differentiator.

Of course, in addition, we are going to choose indications thoughtfully and with the inebilizumab in mind, as you all probably know, inebilizumab has approved in NMOSD and now has positive Phase 3 data in IgG4-RD and myasthenia gravis, MG. And so we're thinking indications adjacent to those or potentially if the opportunity presents itself to follow them into those indications.

On a real molecular level, we think we're probably again better at B-cell depletion than they are. We have a little bit of different way to accomplish ADCC. It's through a low fucosylation versus an afucosylation, we think that provides some advantages.

And then one final point of differentiation is, we do feel that they're under dosing and they have – there's data now suggesting that they're under dosing. They've done pretty rigorous analysis of their PK/PD in NMOSD showing that when B-cells are returning in those populations that those patients are having attacks in NMOSD. And you have to remember when that drug was developed, they were thinking about 90% B-cell depletion.

But we know now that you need that full B-cell depletion. So we have the ability to really purpose fit our dose for our populations, make sure we're getting full B-cell depletion throughout. And so it's a primary goal for our therapeutic development, not to under dose to make sure that we're hitting those therapeutic doses. Something that, that inebilizumabmay be falling a little bit short of having patients return B-cells between say six and – three and six months after treatment.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Could you also just maybe touch on this concept of depletion versus inhibition? What are pros and cons? What led you to choose the depletion approach?

<<William Bonificio, Interim Chief Business Officer>>

Depletion versus…

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Inhibition.

<<William Bonificio, Interim Chief Business Officer>>

Yeah. Like Zenas – yeah, yeah. I mean we think it's – it really comes down to better efficacy. So there are other approaches to inhibit B-cells. There's a company Zenas that has a CD19 that on the other end the Fc is mutated to Fc gamma RIIB, which is inhibitory receptor on B-cells.

And we just – as you look at, we can do some cross trial comparisons as to the effect that has on B-cells. And for example, one biomarker here would be IgG4, immunoglobulin 4 and obexelimab from Zenas. They do have data in IgG4-RD where they were showing say a 36% decrease in IgG4.

And we have our own data in MN showing say a 90% decrease in PLA2R, which is a prototypical IgG4 autoantibody. And we think of course 90% is better than 36%, but we're seeing complete remissions in our data set and we've seen other data, it said like 36% reductions of PLA2R, for example, and those patients would not get remissions, just doesn't have the – it just doesn't have the effect to see those outcomes.

And then as we think again, like Fc gamma RIIB is actually down regulated in autoimmune populations, including SLE, where patients who have mutations of Fc gamma RIIB are actually most at risk for SLE. So it's kind of like the worst population to go after. And they may argue a

safety argument, but as we think about the safety of our mechanism, anti-CD19 monoclonal antibody, it's actually been proven to be very safe with inebilizumab.

They now have long-term experience in NMOSD showing that the safety profile looks very much like rituximab, a drug that is well established, well used, no real concerns. And as that drug was launched during COVID, they took a close look at say humoral immunity, immunity to COVID, childhood vaccine titers, and they're unchanged. And infections don't get worse over time, over those three years, and so overall, very safe profile. So we don't think that the inhibition affords any real advantage in that domain. So again, just better efficacy and similar safety.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Got it, got it. Then how are you guys looking at the opportunity set, right? I think you categorized the indication in certain way. If you can just reframe for us, like what are the indications you are going after and then also maybe touch or put in perspective the MN data that you have generated.

<<Aoife Brennan, President and Chief Executive Officer>>

Yes. So we have disclosed that we're pursuing three different indications. And as we think about there are a broad number of people suffer from B-cell mediated diseases. So the opportunity is really immense. So you have to some way that we can kind of rationalize among all of these diseases, how are we going to select ones that we're going to pursue with this antibody that could really address a really broad population of patients.

And when we took an approach of choosing, we categorized these B-cell mediated diseases into three different groups. And the first group is the IgG4 mediated diseases. And Bill already alluded to the importance of IgG4 in the B-cell and mechanism. So IgG4 is a subtype of immunoglobulin. And what's important about IgG4 is that all B-cells that secrete IgG4 are CD19 positive.

So it's an exquisite immune diseases that are based on an IgG4 mechanism are really exquisite targets for B-cell depletion with the CD19 antibody. And MN is a great example of an IgG4 mediated antibody disease where the antibody is an IgG4 subtype and where when you deplete the B-cells, you see that the antibody levels fall very rapidly to zero.

IgG4-RD for instance is a good example of that, that disease has been very well treated with UPLINZA. They put out very stunning data from their Phase 3 study. So there's a category of rare diseases where the driver is an IgG4 autoantibody and MN is a disease that we're pursuing as an indication and some example of the disease in that set. There's a number of other diseases that could be pursued there.

The second category is what we call the single organ IgG1, 2, 3 disease and that's they're often rare diseases where it's a single pathogenic antibody that's driving the disease mechanism. ITP is

a great example of that, where there's an antibody that's driving destruction of the platelets, you get low platelet count, patients suffer bruising, bleeding, and consequences.

And we think that that's a great indication for us to pursue. But it also helps unlock opportunities in other rare single organ indications where the driver of the disease is an IgG1, 2, 3 antibody.

And then the third group is what we call systemic rheumatologic or complex systemic diseases. There are diseases where often there's multiple organ systems involved, frequently there are multiple pathogenic antibodies. There are complicated diseases, complicated development paths, but huge unmet need.

If you can do something that's transformative for those patients, there's a huge commercial opportunity, diseases like SLE, systemic sclerosis, huge burden from a public health perspective. SLE is a great indication there. And we're pursuing currently a Phase 1b study looking at B-cell depletion in SLE to really answer some fundamental questions about CD19 as a mechanism and whether we can generate responses similar to what's been demonstrated with the CAR T based approaches in terms of being able to achieve something that looks like an immune reset or being able to kind of get deep depletion, such that when the B-cells come back, they're of a naïve phenotype.

I think that's a really important question of can you achieve that with a naked antibody based approach that doesn't have the baggage that a complex cell based therapy has. Because if you can do it with the naked antibody based approach and even a subset of patients, we think that could be a really important advance for these complex rheumatological diseases.

So our three indications that we're pursuing are kind of leads or beachheads in each one of these three areas and I think unlock other opportunities within each one of the categories, if you will. I think the second part of your question is around the data that we've already demonstrated. And I think it really illustrates the point that I was making earlier about what a good target IgG4 mediated diseases are for CD19 based depletion.

So the biology of IgG4 based antibody diseases are that these B cells that produce IgG4 antibodies are very short lived. So when you deplete them, you often get patients into a remission such that you don't necessarily have to continue to give the drug over time, you can deplete all the pathogenic B cells, when the B cells come back, they don't necessarily produce the pathogenic antibody again. We did a small study. It was done by the prior sponsor, the prior owner of the asset. We had eight patients who were dosed, we had long-term follow-up on five of those eight and we had really interesting data. We saw that we were able to achieve B cell depletion in all of the patients. We saw a rapid decline in the pathogenic antibody, which is PLA2R in these membranous nephropathy patients. We saw a rapid decrease in the proteinuria. These patients often present with very, very high proteinuria levels. So they get nephrotic syndrome, often they present with edema, frothy urine, they get very high cholesterol, clotting, things like that.

We saw this very rapid decrease in their urinary protein and we were able to achieve complete responses in 60% of the patients that had data at 48 weeks, which is a really impressive result in

this indication. And what was even more impressive was that these patients appeared to maintain that response over time. So even after the B cells started to come back, the urinary protein levels stayed in the normal range, which I think gets to this kind of concept, that you may not need to maintain B cell depletion.

If you give these patients a good dose, you may be able to allow them to recover in terms of their B cells come back and monitor them over time such that you don't necessarily need to continue to give the product, which I think could be a really great advance in treatment of these immune based diseases. These patients don't need to take long-term immunosuppressants in all cases. And I think that's particularly true for the IgG4 disease set. And the data that we have in pMN kind of indicates that that could be a really interesting opportunity for budo.

<<William Bonificio, Interim Chief Business Officer>>

And just to comment on those data, I think MN is a really nice kind of battleground indication where we have data now from anti-CD20s, anti-CD38s, FcRns, [indiscernible] (0:15:46) and CD19. And as Aoife said, our 60% complete remission rate in that disease at one year is the best data that have been generating in that disease. So better than all those mechanisms I just mentioned and proving that CD19 is potentially the best antigen to target for these B cell mediated diseases and better than all of those competitors.

In addition, as she said, the durable responses are remarkable. So we have patients who are now two years past dosing who are still in complete remission without any drug or any additional therapy on board. So we're quite proud of the data set and we think as we continue to generate data, we'll see this be recapitulated in every other indication that we go after.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Got it. What are the next step now? I think for each of these indications, you're starting a Phase 2 program. Do you have to do dosing work? Just maybe talk about the scope and the size of the studies?

<<Aoife Brennan, President and Chief Executive Officer>>

Yes. So we've guided to initiation of two trials. The first one is an SLE study. We just announced yesterday as part of earnings that we now have an open-IND. So we've kind of gotten off to the races there with that, that we're starting to set up all of the sites and we've guided to dosing our first patient in the first half of next year. That study will be a dose escalating study, where we'll start off with the low dose and escalate over time. Really to find the dose that depletes B cells and maintains B cells depleted throughout that first dosing interval in SLE patients. They're a bit of a unique population in that these patients are on concomitant medications, they frequently have high disease burden.

These are patients with severe SLE coming in with active disease and we're really going to be looking for the dose that can get those B cells down in a high sensitivity assay and looking at what happens when the B cells come back. Do we see this naïve phenotype? Do we see the

antibody depletion? What happens clinically to their disease activity in this highly active disease population? So that's going to provide some really interesting readouts. It's an open-label study, so we'll be accruing data as we go along and dose patients.

The second study that we've discussed and shared some thoughts on as part of our Investor Day recently is our study in ITP. So that's a single arm open-label study as well, where we're going to be doing some dose exploration there. We'll be taking patients with chronic ITP. So these are patients who've failed a standard of care therapeutic, who've had ITP for a period of time and are not responding and will be giving them a CD19 depleting antibody and looking at what happens to their platelet counts. Do the platelet counts recover? It's a really nice indication, because you have a very measurable endpoint. The placebo response rate is very, very low in these chronic ITP patients.

So we do think we're going to get some really interesting data on platelet counts, again, it's open-label. So as we start to accrue patients, we'll be able to generate some data from that study. And then the next steps for pMN will be to move into a confirmatory phase of development with that program. And we'll be sharing additional guidance and information as we finalize plans for next steps with that program as well.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Very good. Are the dosing different for SLE and ITP and how they are relative to the dose that was studied in MN?

<<Aoife Brennan, President and Chief Executive Officer>>

We don't know that yet. Yeah, that's to be determined. It's possible, but we just don't know that.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Okay.

<<William Bonificio, Interim Chief Business Officer>>

I guess, just for context, with the MN, originally the first in human oncology, we went up to 1,000 milligrams by four doses. So that's 4,000 milligrams or 4 grams of the drug. And it was not reaching a maximum tolerated. We did not reach a maximum tolerated dose even at that. There was no remarkably at that level. In MN, we studied it at 100 and 200 milligrams by two weeks at weeks 02 and then weeks 24 and 26. And at those dose levels, we saw some complete and durable depletion of B cells. But we had a couple other patients who were coming back between weeks 12 and 24. And we see that also with inebilizumab, some percent of the population come back. And so we just want to make sure we nail that dose level to make sure that all the patients are fully depleted throughout the course of therapy. And we're going to work on building a robust model, a PK/PD model to make sure and ensure that we do that. Depending on the indication, again, depending on…

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Yeah. These are all Sub-Q dosing that you are evaluating and what is the formulation or what work you need to do to get to Sub-Q.

<<Aoife Brennan, President and Chief Executive Officer>>

So right now it's IV dose. So we do have a subcutaneous formulation, we shared some information on that recently as well. We've achieved a concentration of **175** mg/ml. So we finalized a subcutaneous formulation presentation. We're moving that now into in vivo studies in animals. We'll be sharing some data from those work – those studies in next year and then if that looks good, moving it into clinical trials. So that will be kind of trailing behind the IV program. So slightly that the studies that I've just discussed will be completed with the IV formulation and then the subcutaneous would be kind of follow on for me.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Okay. Follow on, okay. I have a question on the ITP side. I think if you look at the currently approved drugs, the commercial outlook is not that great. Like, what do you think is the issue and what are you aiming to show with this mechanism?

<<Aoife Brennan, President and Chief Executive Officer>>

Yeah. When you look at the drugs that have recently been approved, the efficacy has been anemic and that's kind of [indiscernible] (0:21:04).

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Understand, yeah.

<<Aoife Brennan, President and Chief Executive Officer>>

But when you think about what happens right now for a patient who is diagnosed with ITP, usually, they get treated with steroids, then they get rituximab. Rituximab works first time, right, about 50% of patients will get a response. The problem is that most of them will have a relapse within two or three years. They get another treatment with rituximab, they get about 50% respond to that and then they continue to relapse. Then the next line is TPOs, where essentially you're flogging the bone marrow, right? So that's not getting to the underlying pathophysiology necessarily or chronically taking this TPO agonist. There have been a number of products that have come out subsequently to rituximab.

And most of them have, in this kind of chronic ITP indication, and even recently, there's another data set from a Phase 3 study that's come out and most of them look very, very similar in their Phase 3 studies where the placebo group almost zero responses and the active group is around 20%. And so these are products that have to be taken chronic immunosuppressant, where you're getting a 20% response rate.

So I think that's not a great value proposition, I think for most patients and physicians. And what you'll hear when you speak to physicians is like, why would I do that when I can get like an 85% response rate with splenectomy or I can get a 40% to 50% response just giving them another dose, of course, of rituximab, which is now generic. So I think, it's not surprising to me that the commercial performance of those recent products hasn't been stellar.

So I think you have to have – if you can put up something that's a genuine contender that can achieve better response rates and more durable responses than rituximab, which I think based on the pathophysiology of CD19 depletion, we should be able to do. I think it fundamentally addresses the underlying pathophysiology of the disease. It gets more patients into remission and allows more patients to remain disease free for longer.

That's fundamentally a different value proposition than telling someone you have to remain on long-term immunosuppression or you're going to be on long-term TPO agonist where you're going to be at risk of clotting and everything else. Like, it's a very, very different paradigm in terms of what you're telling a physician or a patient. And I think if you can demonstrate that a CD19 is a better rituximab, then I think gradually what you'll see is you'll see that rituximab will be displaced as first line over time, right. Because why would you take something that's 50-50, if you can get to an 80% and a much better durable response compared to a CD20?

And certainly, the pathophysiology of ITP demonstrates that in those patients that break through CD20, a lot of that breakthrough is due to CD19 positive cells in the spleen. So you're depleting the CD20 positive cells, but what's left behind is these CD19 positive cells producing the antibodies. So I think there's good reason to believe and we have a very high bar for what like going into a Phase 3 would look like. If we're putting up another 20% product, that's just not going to be good enough. I think we're really going to want to see something that's going to be impressive for patients and physicians.

<<William Bonificio, Interim Chief Business Officer>>

And those commercial dynamics are playing out right now in NMOSD with inebilizumab where it has taken over rituximab as a frontline standard of care. In fact, that's a competitive market with complement and IL-6 approved. And yet CD19 being the best therapy, better than rituximab, better than these other agents, is used frontline is doing 400 million a year in a population of around 10,000 patients and is working in those patients that failed rituximab and would have otherwise not been able to be treated. And we saw in our MN study, patients who had failed rituximab entered our study and had complete remission had durable remission. So it's all sort of playing out exactly as Aoife mentioned.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

So you have a lot that you could do just with CD19, but you did mention about the BD capabilities. What is your appetite for that? How are you thinking, how active you are?

<<Aoife Brennan, President and Chief Executive Officer>>

So I think there's a number of interesting opportunities now that we're going to be keep our eyes open for, we have a pretty high bar. We got a great asset in budo and with a really interesting kind of opportunity set. If something similar comes along, we'll definitely jump on it. And Bill is constantly looking…

<<William Bonificio, Interim Chief Business Officer>>

In former lives, never stop PD always look and so…

<<Aoife Brennan, President and Chief Executive Officer>>

Always be looking. Yeah. So be the first to know.

<<Yatin Suneja, Analyst, Guggenheim Securities>>

Very good. Thank you. Thank you so much.

<<Aoife Brennan, President and Chief Executive Officer>>

Great.

<<William Bonificio, Interim Chief Business Officer>>

Thank you.

<<Aoife Brennan, President and Chief Executive Officer>>

Thanks for the invitation.