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<<Umer Raffat, Analyst, Evercore ISI>>

[Call Starts Abruptly] you, guys for joining us. Super excited to have management team from Climb Bio. Some of you might remember them as Eliem Therapeutics and they've been rebranded. So maybe Brett, let's just start there. What was Eliem? What's Climb? And we can jump right in.

<<Brett Kaplan, Chief Operating Officer>>

Yeah. First of all, thank you, Umer for hosting us. Always good to be back with people I used to work with and good friends. Thank you.

<<Umer Raffat, Analyst, Evercore ISI>>

Absolutely.

<<Brett Kaplan, Chief Operating Officer>>

So Climb, very interesting story, but has a more interesting backstory. Previously we were Eliem Therapeutics, which is a RA-backed neurology company that was looking for strategic options and ultimately decided to acquire another RA company called Tenet Medicine. Tenet Medicine had acquired out of ACELYRIN, budoprutug, which is our core asset now anti-CD19 monoclonal antibody. And the deal closed together with a pipe mid this year and RA decided to bring in some management around the assets and brought in myself and the CEO, Aoife Brennan.

And we also have the Interim Chief Business Officer, Bill Bonificio, who's on the team for now. And we have this exciting opportunity to build an I&I company centered around this monoclonal antibody, budoprutug. Budo's got a long history for the backstory here. It was originally founded by Merck KGaA, as an oncology asset and it's helpful in that we have data was also then passed on to Cancer Research UK, landed up at ValenzaBio, then into ACELYRIN and then back to Tenet and into us, data in oncology went up to 1,000 milligrams and a very safe asset in that respect.

Valenza had then developed the compound initially in membranous nephropathy. So we have Phase 1b data in about five patients and have a 60% response rate which is unique and archetypal. So very exciting data in membranous nephropathy, which is an archetypal IgG4 disease, where we think this asset is very well positioned. We can get into what else we're developing. But that's the backstory on the company. We are well capitalized just from a financial perspective with over $200 million in cash and financed through 2027. So a lot of money to do a lot of good things here.

<<Umer Raffat, Analyst, Evercore ISI>>

Got it. So I guess, the one liner explanation of Climb Bio would be Uplizna but for different indications. Would you agree with that?

<<Brett Kaplan, Chief Operating Officer>>

For now for sure. I think we have the advantage of Uplizna paving the way for us. So for those that don't know Uplizna, this is the Amgen's previously Horizon CD19 antibody with approved in NMOSD with Phase 3 data both in MG as well as, I'm going to go blank on the recent data but so two positive Phase 3 trials paving the way for us, certain limitations around that asset in the weight was developed not so much in terms of the asset itself.

And we think we have some advantages in what we can do both from a dosing perspective. So we can dose to B cell depletion, but we also have the advantage of being able to develop a subcu formulation. So we've achieved a 175 milligram per mill subcu formulation which could have advantages especially in the more chronic diseases. We believe Amgen had tried to co-formulate Uplizna assay subcu but weren't able to get there.

<<Umer Raffat, Analyst, Evercore ISI>>

So maybe let's start there. So CD19 antibody Uplizna and then your CD19 which was developed by Merck, right?

<<Brett Kaplan, Chief Operating Officer>>

Yeah.

<<Umer Raffat, Analyst, Evercore ISI>>

So you said, they can be not subcu, you guys are. Is that because the dose is different?

<<Brett Kaplan, Chief Operating Officer>>

I think it comes down to the connects of the antibody itself and ability to formulate. They are an afucosylated antibody. We are low afucosylated antibody, but both use ADDC. It just comes down to certain technicalities around the formulation, the antibody itself.

<<Umer Raffat, Analyst, Evercore ISI>>

And what about the binding affinity to CD19?

<<Brett Kaplan, Chief Operating Officer>>

So if you look in preclinical studies, we believe we have about a 5x to 10x greater potency. When you look at comparable preclinical models…

<<Umer Raffat, Analyst, Evercore ISI>>

10x potency.

<<Brett Kaplan, Chief Operating Officer>>

Yes, potency advantage, whether that will translate to clinical benefits, time will tell. But more importantly, I think our advantage is not so much in the potency but more in the ability to just to go after different indications and also the Sub-Q part.

<<Umer Raffat, Analyst, Evercore ISI>>

And remind me, the dose Amgen used? What dose and what doses are you guys using? I realize it different indications.

<<Brett Kaplan, Chief Operating Officer>>

Yes, we're using – well, right now the dose that was studied in the Phase 1b membranous nephropathy study was 100 milligrams and 200 milligrams given twice at day zero and day 14, and day 26, and day 28 – week 26 and week 28, so four doses total.

<<Umer Raffat, Analyst, Evercore ISI>>

Day zero, 14, 28 and then…

<<Brett Kaplan, Chief Operating Officer>>

Day zero, day 14 and then week 26 and 28. Sorry. Yeah.

<<Umer Raffat, Analyst, Evercore ISI>>

And then every six months from there.

<<Brett Kaplan, Chief Operating Officer>>

Well, we didn't dose beyond those two.

<<Umer Raffat, Analyst, Evercore ISI>>

Okay, got it. Okay. And what was Amgen dose?

<<Brett Kaplan, Chief Operating Officer>>

I don’t know.

<<Umer Raffat, Analyst, Evercore ISI>>

Okay, got it. All right. And in terms of B cell depletion can you walk us through your data?

<<Brett Kaplan, Chief Operating Officer>>

So the early data shows not only rapid B cell depletion, but we also have the anti-PLA2R antibody depletion. So we have which is the marker for membranous nephropathy that targets the glomerular cells. But we also have a complete response, so a clinical response in terms of proteinuria reduction in these patients. So we have both the biomarker – the CD19 biomarker, the B cell depletion, the antibody response, and then the relevant clinical biomarker here.

<<Analyst, Evercore ISI>>

Brett, what do the B cell repletion kinetics look like at this point?

<<Brett Kaplan, Chief Operating Officer>>

So in some of the patients – so this is a very interesting topic and it’s becoming a very – it’s a lot of new interest in terms of diving deeper in not just what type of in B cell repletion, but the type of B cells that are coming back, whether they naive or disease pathogenic B cells. What we show in some patients we do get B cell repletion, I think around about the six month mark is, which is why we dose again at the 26 week mark. I think if two or three of the patients did deplete, but despite that we were able to get disease complete response.

<<Analyst, Evercore ISI>>

Right. And I realized that the fact that all five patients had at least partial responses is great. But until those patients who did not, could that be due to partial B cell repletion at six months or no.

<<Brett Kaplan, Chief Operating Officer>>

Not clear. It could be. So we need to figure out if those are pathogenic B cells or not. But again, yes, this is something we’d have to explore further, which we would like – which we will target in our ITP and SLE studies going forward.

<<Umer Raffat, Analyst, Evercore ISI>>

Got it.

<<Brett Kaplan, Chief Operating Officer>>

But certainly I think this concept of immune reset is one that is interesting. We believe it’s a bit more complicated depending on the disease type. But we do see – we do believe that unlike some

of the inhibitory B cell agents out there, depleting B cells greater than 90% is key. You need to knock down, especially in the short lived diseases like MN, where if you can knock down the B cells and hopefully reset the immune system, even if they come back, they are naive.

<<Analyst, Evercore ISI>>

Got it.

<<Umer Raffat, Analyst, Evercore ISI>>

Brett, I would have thought you guys should go after myasthenia gravis with another trial, maybe do it a little different. Amgen did steroid taper. You just do it without steroid taper, you might even end up with better placebo adjusted efficacy. And it's such a large emerging market that it would probably make sense to have a follow on to a placebo there as well. I'm just curious how you guys think about that. It sounds like that's not on your indications.

<<Brett Kaplan, Chief Operating Officer>>

So the way we thought about indications and I'll get to myasthenia gravis as we divide them into three buckets. We're targeting IgG4 diseases. So this is where membranous nephropathy falls in. We then look at the IgG1 to IgG3 diseases. This would be an ITP type disease. And then we're looking at more complex systemic diseases which SLEs a beachhead for us. Each of those have a different risk profile with MN being the least risky out of all the diseases. We think the mechanism should work in all. But there's an execution and a patient risk associated with them.

So – but to your – so that's how we think about it. So certainly as we think about myasthenia gravis, we think about a lot of indications for systemic sclerosis, myasthenia gravis and could all be additional indications. We just got to figure out execution timing and can we be differentiated versus Uplizna in that setting.

<<Umer Raffat, Analyst, Evercore ISI>>

So you guys are not saying no, but it's not the base case plan right now.

<<Brett Kaplan, Chief Operating Officer>>

Right now it's not in the base case operating plan. But part of our strategy is certainly indication expansion beyond these three indications. And BD looking at additional assets outside of CD19 is a big part of our strategy.

<<Umer Raffat, Analyst, Evercore ISI>>

I guess, what if you guys were able to get access through BD to a FcRn of sorts and you run a trial of FcRn plus this and basically have a one stop shop where you do FcRn for the early part and then the maintenance within every six months.

<<Brett Kaplan, Chief Operating Officer>>

Yes, I think combination therapy, whether it's within FcRn or even I think some people would consider looking at TCE combinations, TCE combinations could be interesting. I think there are a lot of possibilities in terms of combination therapies. Don't know about the regulatory pathway for developing them, but certainly interested in that. I wouldn't say it's top priority. We probably look at other assets versus combination therapy first.

<<Umer Raffat, Analyst, Evercore ISI>>

Got it. Okay, great. And when you say TCE, you're talking about CD19 bispecific?

<<Brett Kaplan, Chief Operating Officer>>

Yeah. So T cell engager.

<<Umer Raffat, Analyst, Evercore ISI>>

Okay, but why would that make sense as a company?

<<Brett Kaplan, Chief Operating Officer>>

There is a theory potentially that you can knock down the B cells, say starting with the CD19, reduce your inflammatory response and then come in later with a more potent T cell engager afterwards. So there's a way to think about combination therapy that way.

<<Umer Raffat, Analyst, Evercore ISI>>

I'm just thinking out loud. You take CD19, B cells go down, then you take a T cell engager to take them down even more?

<<Brett Kaplan, Chief Operating Officer>>

Even more and get it CD19…

<<Umer Raffat, Analyst, Evercore ISI>>

And would be lesser in that case.

<<Brett Kaplan, Chief Operating Officer>>

Correct. I'm not saying we're doing it, but there are many ways to think about combination therapy.

<<Umer Raffat, Analyst, Evercore ISI>>

And speaking of CRS, could you remind with a CD19 naked antibody, is there any risk worse?

<<Brett Kaplan, Chief Operating Officer>>

So we have both our data that at Uplizna has both commercial and Phase 3 data showing the products are extremely the CD19 molecular antibody is extremely safe. No CRS. Even the, I think, even in our Phase 1 study, we had limited infections. This was these patients was during COVID. So three out of the five patients have developed COVID. So this is unrelated to any of the perceived safety risks around B cell depletion. Remember, because of CD19 doesn't get to plasma cells, it gets to plasma blast, but not plasma cells.

Our safety, our humoral safety is much greater than, say, a BCMA, CD38, or any of those molecules that are targeting plasma cells themselves. So infection risk is not a problem. And we know that even when you look at the Amgen data, it costs thousands of patients.

<<Umer Raffat, Analyst, Evercore ISI>>

Got it. So maybe let's dig into your data, then remind us. You said you have five patients in membranous nephropathy.

<<Brett Kaplan, Chief Operating Officer>>

Five patients in membraneous nephropathy dosed between 100 milligrams. There are two dosing cohorts, 100 milligrams and 200. Unfortunately, this study was started before we got the asset and went. This was, I think, under the Xceleron umbrella. So the study was stopped before we acquired Tenet. Five patients developed – five patients, of which three had a complete response and two had a partial response. This is unprecedented data.

<<Umer Raffat, Analyst, Evercore ISI>>

Oh, three had. Well, I thought one was effectively cured.

<<Brett Kaplan, Chief Operating Officer>>

No, three had a complete response and two didn't. Yeah.

<<Umer Raffat, Analyst, Evercore ISI>>

Three had a complete response and…

<<Brett Kaplan, Chief Operating Officer>>

50% complete response rate. Yeah.

<<Umer Raffat, Analyst, Evercore ISI>>

And remind me again, because I know there's so many different modalities going after some of these kidney indications right now. What else is in the pipe for membraneous nephropathy?

<<Brett Kaplan, Chief Operating Officer>>

I think several have failed in membraneous nephropathy, but I don't know the list of other competitors right now.

<<Analyst, Evercore ISI>>

Okay, makes sense. Makes sense. I remember we were discussing dose, and one of the points you had said for your autoimmune doses, it's 100 milligrams and then or 200 milligrams. But in oncology, the dose was 1,000 milligrams. Could you walk us through the dynamics on B cells between these...

<<Brett Kaplan, Chief Operating Officer>>

We get complete B cell depletion with 100 milligrams within a few days. So – but we know we're way below a potential top maximum tolerated dose. So we've got a lot of room to explore here. Each disease is going to be different. Remember in membranous nephropathy you've got leaky kidneys. So despite even – despite 100-milligram dose and a leaky kidney we're still getting complete B cell remission. That being said, I think the way I view our ITP and SLE studies is we have an advantage to explore different dosing, potentially higher doses.

<<Analyst, Evercore ISI>>

Got it. Okay. Makes sense. And then maybe the, as we switch to your next indications and the trials you guys are initiating, maybe walk us through. You guys haven't run a trial yet?

<<Brett Kaplan, Chief Operating Officer>>

Not yet, no. So we have, we announced that we have opened an IND for SLE, so that will be first patient end in the first half of this year. I think we all realize in this room, well, those of us close to the SLE game, this is a competitive space. The FDA in the certainly in the room division is stringent. So this is going to be, we're no different to any other company that's starting an SLE trial. It's going to be take time but the market at the back end is pretty significant and we think the drug has certainly an advantage compared to other targeted agents out there. So that will be one of the trials starting this year in 2025, sorry, the next...

<<Analyst, Evercore ISI>>

And so this will be randomized or...

<<Brett Kaplan, Chief Operating Officer>>

Placebo controlled. I mean, open label, sorry, open label Phase 1b.

<<Analyst, Evercore ISI>>

Okay. Open label phase 1b. Okay.

<<Brett Kaplan, Chief Operating Officer>>

But single day standing dose...

<<Analyst, Evercore ISI>>

And should we also every six months type dosing?

<<Brett Kaplan, Chief Operating Officer>>

We haven't discussed dosing yet, yeah.

<<Analyst, Evercore ISI>>

Okay, got it.

<<Brett Kaplan, Chief Operating Officer>>

But most likely that would be the type of dose you would look at.

<<Analyst, Evercore ISI>>

Excellent. Brett, I know that Tenet had originally started to design a Phase 1b2a trial in SLE that got withdrawn. Any learning from that or could you comment on how you're doing things differently in this upcoming study?

<<Brett Kaplan, Chief Operating Officer>>

So I think we – you take FDA feedback and it's a negotiation. But I think as I said, FDA certainly the room division is particularly concerned about some of the agents safety out there and I think they bucket lump many of us together in that concern. It's there's so much – there's limited wiggle room you have with respect to the agency. But I think we are going to play by the rules here and we'll try to utilize a global trial to, to accelerate the data here. But it is from a U.S. perspective just it is what it is for now.

<<Analyst, Evercore ISI>>

I see. Okay. ITP. I know there's a lot of interest on the CD38 side to go after that target as well. I guess, what's the plan? Because I wonder at some level the ultimate winners in these spaces will be whoever is the first one to get something over the line in the end and I guess what level of urgency are you guys moving within these very competitive indications?

<<Brett Kaplan, Chief Operating Officer>>

We think CD19 is particularly well suited for ITP. If you look at the rituximab data, those patients that relapsed their spleens are full of CD19 positive B cells. So unlike a CD20 drug, we think we have the advantage of actually getting into the tissues here and potentially having a more efficacious response rate. That being said, if you look at efficacy data across multiple different trials, the response rate is about 20% to 30%. So bar is pretty low even, so, but yes, it is competitive. That being said, we think we know Rituxan works reasonably well. We have the extra edge of being able to get into the spleen and getting into – not getting into the spleen, but treating CD19 positive cells here. So there is a clinical advantage without the potential safety concerns of the CD38s or the TCs, et cetera, that are going after this.

<<Umer Raffat, Analyst, Evercore ISI>>

Got it.

<<Brett Kaplan, Chief Operating Officer>>

And if you, I think you know, the right. Several coming, I think are struggling still with ITP. It's a tough disease.

<<Analyst, Evercore ISI>>

Brett. I know Climb Bio in the past, in the recent past, kind of just commented on the heterogeneity of patient responses in ITP. So kind of how do you plan to tackle that, if anything, in the future?

<<Brett Kaplan, Chief Operating Officer>>

Look, it's going to be, patient selection is going to be critical. Getting people who aren't at the end or burnt out, I think is going to be a big part. Making sure you don't have, that weighted in your study. So initially it's going to be about careful patient selection.

<<Umer Raffat, Analyst, Evercore ISI>>

Sure

<<Brett Kaplan, Chief Operating Officer>>

It does mean that your trials may take a bit longer, but we think the bar, as I said, is pretty low. But, shooting for something ahead of 30% response, should be achievable given this mechanism.

<<Umer Raffat, Analyst, Evercore ISI>>

Got it. So maybe remind us then, Brett, timelines in the last couple of minutes, you guys are starting those trials in first half. When can we get the first clinical updates?

<<Brett Kaplan, Chief Operating Officer>>

We haven't provided guidance on the data. I think you can use math to come to a conclusion there, but it's not going to be in 2025 is what I would say.

<<Umer Raffat, Analyst, Evercore ISI>>

These are 26 readouts?

<<Brett Kaplan, Chief Operating Officer>>

This is a 2026 event, the way I categorize 2025.

<<Umer Raffat, Analyst, Evercore ISI>>

But there will be placebo adjusted.

<<Brett Kaplan, Chief Operating Officer>>

Correct. So there's an opportunity potentially in both the ITP and the SLE cohorts to have data. I think we're very mindful of rolling out single patient data that don't provide a full fulsome set or a view of the potential of the drug. So we aren't guiding to sharing any data in 2025, but that certainly is a possibility, Umer.

<<Umer Raffat, Analyst, Evercore ISI>>

Okay, got it. Excellent. And then nothing on the manufacturing front or anything that hold you guys back from the trial start timelines or anything like that?

<<Brett Kaplan, Chief Operating Officer>>

No, I mean we are working through the CMC, but this is not a, a rate limiting step for us. As I said, ITP and SLE will certainly start in the first half. We haven't guided to when the more advanced studies in MN. So these aren't going to be Phase 1. These are going to be advanced clinical studies in MN will start. We also will provide data in 2025, non-clinical data on our subQ formulation and we'll plan to start Phase 1 studies there.

<<Umer Raffat, Analyst, Evercore ISI>>

Makes sense. Excellent.

<<Analyst, Evercore ISI>>

And are you completely finished with your subQ work? Is it wrapped up at this point, Brett?

<<Brett Kaplan, Chief Operating Officer>>

No, still we are working through that and rolling it out. So we'll have the non-human primate studies because you have to do talks on the subQ, but it'll be ready for Phase 1 studies in the near term.

<<Analyst, Evercore ISI>>

And are you kind of formulating by yourself? Are you kind of partnering with a third party formulation?

<<Brett Kaplan, Chief Operating Officer>>

We use third parties to help with the formulation, but we have a 175 mg/ml formulation. So two mls will give you 350, which is a pretty substance of those front.

<<Analyst, Evercore ISI>>

Got it. Got it. Now this is for me, Brett. Umer anything else?

<<Umer Raffat, Analyst, Evercore ISI>>

No, I think we covered it all.

<<Brett Kaplan, Chief Operating Officer>>

Thank you. If there any questions from the audience? Awesome. Thank you guys.