[BEGINNING OF Climb Bio, Inc. (CLYM).mp3]

Yasmeen: ...into our Piper Sandler Healthcare Conference. My name is Yasmeen Rahimi. I'm a senior biotech analyst here at Piper Sandler. Really excited to have the team from Climb Bio at our conference. Thank you so much for being here.

Bill: Yes, you're welcome. Thank you for having us. Here's Aoife right now.

Aoife: [inaudible 00:00:18.248].

Bill: Can you get her a mic? They started without... They had to start, they said.

Yasmeen: Yeah, perfect. I think while we're waiting, it would be wonderful to give a little bit of a history around the assets...

Bill: Yeah. They have to do that.

Yasmeen: ...the formation of the company.

Bill: That's a good place to start. Yeah.

Yasmeen: I think that's a good place to begin.

Bill: So I can give a little history on the asset itself and I think Aoife can fill in when she's joined, which is more recently. So Climb is a single-asset company. We're developing an anti-CD19 B cell-depleting antibody called budoprutug that has enhanced effector function and depletes B cells. This asset was originally developed by Merck Serono and originally developed for oncology. It was initially brought into a population of folks with B cell malignancies in first human studies by Cancer Research UK in partnership with Merck Serono. After that study, the study was dosed, the drug was

doing what it was supposed to do. It was clearing B cells in those patients. Some of them had good responses, in fact, to that drug.

And of course, Cancer Research UK was not going to advance this into phase 3 pivotal studies in oncology. So they put it up for license. And it was at that time that I was part of a team that in-licensed for autoimmune diseases. So we licensed at a company called ValenzaBio, which was later acquired by a company called Acelyrin. And it's from Acelyrin where we more recently got this asset. So in the beginning of this year, we licensed this program, Budoprutug. In fact, acquired this program, Budoprutug, from Acelyrin, acquired the license from Acelyrin. And with the idea of continuing to develop it in autoimmune diseases, at Acelyrin, they were getting additional data that were looking really good in membranous nephropathy, which we can talk about. And that was the impetus to go out and back and get it. And with the asset in hand, we did a merger deal with a company called Eliem along with a concurrent pipe of $120 million in addition to the cash Eliem had, gave us a total balance sheet of $200 million. And right now, as of September 30th, $218 million. But it was that story that Aoife kind of walked into, the CEO. So Aoife, please, you can take it from there.

Aoife: So I got a call around June to say there was this interesting asset, a shell private company that was tenant. So I met Steven and Bill as part of that. They had this interesting asset with an interesting data set and this very well-funded public shell with the pipe coming along as well. And of course, that's an opportunity that doesn't come along very often, building a management team from scratch with all of those resources. And I think concurrent with this, you know, I think Bill has been very modest. But I really do give him a tremendous amount of credit because they had a huge foresight in seeing the potential of CD19 before really anyone else did.

I mean, it was really only earlier this year with some of the CAR-T CD19 data that, you know, the attention really of a lot of people in the I&I space started to really appreciate CD19 is differentiated from other B cell targets. It really is differentiated from CD20 and I&I. And I think it took some of the early CAR-T data for people to start sitting up and paying attention. Up until that point, I think CD19 was very underappreciated as an interesting target. We've now seen the Amgen data read out multiple positive phase 3 studies in different indications demonstrating really best-in-class efficacy with a very good safety profile across a number of

different indications, which I think is very validating of this kind of CD19-based approach. And I think the team of tenants kind of recognized that, had been following this asset for a number of years and kind of saw the potential to take this kind of unloved, shelved asset and build a company around it. And I was really fortunate to be tapped on the shoulder to be part of the story earlier this year and actually building a company around this really interesting clinical stage asset.

Yasmeen: That's wonderful. What led to the decision to move forward the asset and to MN, ITP, and SLE?

Aoife: Yeah. So the MN study was actually performed prior to the asset coming in, but I think it was a really good decision. MN is a prototypical IgG4-mediated disease. And unlike IgG1 to 3 diseases, all B cells that produce IgG4 antibodies express CD19. So when you deplete CD19 positive B cells, the antibody levels decrease very precipitously. So you get this really nice readout, and that really reads through very nicely to the clinical end point. So in terms of choosing MN as the initial indication for B cell-depleting CD19 antibody, it made tremendous sense based on the biology and those biomarkers. You can really clearly follow.

I think the second component of why PMN is a very interesting indication is that it's really, I think, the next rare renal indication that is, I think, going to be developed as a commercial opportunity. There's no real FDA-approved therapeutic that's been developed. It's a very well-established market. There's about 100,000 patients in the U.S. It's a very prevalent cause of nephrotic syndrome in adults. There's a big unmet need. These patients often don't respond to current standard of care. So there's a number of patients that can be addressed. So we think it's a really interesting application for us across a number of different axes here, particularly, as a small company. I think it could be very interesting.

So that decision was made prior... I can't take any credit for that. But I think it was a very good one. It makes sense when something makes sense from a biology perspective, from a development feasibility perspective, as well as from a commercial perspective, and kind of checks all three of those boxes. Then when we looked at some of the other places that we could think about exploiting this antibody that we have, the space is really broad. And early on, there was a question about whether, you know, CD19 was really going to be applicable just in this kind of narrow slice of the pie in the IgG4 space, or could it really be used across all B cell-

mediated diseases. We now know, based on the Mint readout earlier this year, that B cell depletion actually can work across all B cell-mediated diseases.

So we now have this kind of broad set of indications to think about targeting. And so it's now a question of, like, okay, how do we think about moving this opportunity forward? And when we look across all of them, we see outside of the IgG4 diseases, we see kind of these two categories. We see the single target organ where there are often rare diseases like ITP, like myasthenia gravis. And some of those indications have well-established endpoints. They often are rare diseases with well-established regulatory approval pathways. We think there's some of those that are still very much kind of open for additional improvements in therapeutic development. And so I think there's indications there that look very interesting to us. ITP is going to be our first indication there, but certainly, there's potential for us to pursue others. We're moving forward with an ITP clinical trial. We're going to dose our first patient there next year. And that would essentially open up other opportunities in that set.

And then I think the final space that's very intriguing is a more complicated space, I would say, which is these kind of multi-organ complex rheumatological diseases, tremendous unmet need. These are patients who often have multiple organ systems involved, multiple pathogenic antibodies, diseases like SLE. They're interesting commercially, big commercial opportunities, very prevalent diseases. Some therapeutic development has occurred there, but still a lot of unmet need. And we're pursuing an SLE indication. We're going to initiate a study in the first half of next year looking at budoprutug in patients with a severe SLE to really understand what the efficacy and safety profile looks like in that population because we really do think that we could potentially do something transformational for patients with SLE as well. So we kind of see that there's opportunity across all of these three categories. And I think the readouts from the early studies will inform which ones we do and take forward as we advance the molecule and the programs.

Bill: And I would only add the decision to continue in MN is informed by the data that we've already generated in that disease. So we really put up best-in-disease data in MN. We had 60% of our patients in our... We ran a phase 1B study and 60% of our patients had a complete remission of disease in that study, which compares favorably to other B cell antigens or B cell-targeting agents such as CD20s and CD38s. And so,

yes, with those data in hand, of course, MN continues to make a lot of sense as our lead program.

Yasmeen: Since we're on... Before we go into MN, like, I think you're going to be starting these three indications. What's the sequence of them? Are you planning to start each of them? Sort of they're all guided from one age, one. And then secondly, I think that data is really encouraging in MN. So have you had regulatory discussions around next steps and how would that study look like? I'd love to maybe think about sequencing and then MN first, given that there's existing data.

Aoife: Yeah. So Bill is absolutely correct. We're a little bit ahead in MN because we do have some very promising phase 1B data. So we have evaluated budo in a phase 1B study in patients with MN where we've demonstrated really interesting early efficacy data and we have safety data on the three of those patients as well. So that's kind of a little bit ahead of ITP and SLE from just a stage of development perspective. What we've seen in MN so far makes us compelled to take that forward into late-stage development. So on the back of the early phase 1B data that we've seen, we really want to start engaging with regulators now about, okay, what does a late phase development program look like in this indication?

We've committed to moving forward with our manufacturing plans and making sure that we have a robust understanding of what that late phase kind of commercial manufacturing looks like and making sure that we have all those ducks in a row, as well as understanding what the path for nonclinical development would require from the BLA perspective. So that one is going to likely be our first program that moves in because we have data that we believe could be, you know, best-in-class for this molecule. The others are going to come a little bit behind, so we'll have go/no-go decisions to make in ITP and SLE. Obviously, unless the data in our first studies looks compelling and competitive commercially, we would make a decision then to move ITP and SLE forward on the back of kind of early data from the studies that we'll initiate in the first half of next year.

Yasmeen: And team, like, when you step back, like, what is the strongest... I guess before we go there, like, historically speaking, what would be the size, duration, end points be for MN study? Yeah.

Aoife: Yeah. So there hasn't been an approved product in MN, but there are studies that are ahead of us that we can use as

a guide. I think the one that I would point to is there's CD20 antibody called GAZYVA with [inaudible 00:12:13.848] Roche. They've just completed enrollment in a phase 3 registration study. So they've disclosed the study, the time, the size, the duration, in terms of how long it took them to enroll. And that study was a comparative efficacy study compared to Tacrolimus, it was about 140 patients. It took them about two years to enroll. That was very small, single registrational trial in that indication. The endpoint was a complete response rate in two years. So it was an endpoint that we understand, but we've already demonstrated a 60% CORH in our phase 1B study.

So I think it's very doable in terms of the size and duration of the study. Unlike other glomerulonephropathies, we understand that there's not a requirement around EGI4, for instance, which can be very challenging in some of these kind of slow, bouldering diseases where often you're required to kind of follow patients for a long time before you see that slope of your EGI4 decline here because we have that kind of complete response rate as the endpoint for full approval. I think it does make it a very attractive disease area for development. And I think I would point you to that as kind of a model for what a phase 3 study would look like in this indication.

Yasmeen: Okay. And then what is, in your view, stepping back, the strongest indication of CD19 working in ITP?

Bill: Yeah, I can answer that. So we know ITP is a single-organ disease, autoantibody driven. In this case, you have autoantibodies to be destroying platelets on that organ as a spleen. We know B cell depletion works here for a number of reasons. First and foremost, rituximab works in this indication. It's part of the standard of care. And in those patients who receive rituximab, about half will have a response to rituximab, maybe 30% to 50%. And it's about that number, 30% to 50%. Every time you use rituximab, about 30% to 50% of those patients will respond. But what's nice in this disease is that splenectomy is also a treatment here, and so patients who have rituximab, if they have rituximab, they often go on to splenectomy. And you can do biopsies on those patients' spleen to see exactly what's happening in the spleen, exactly what's generating those autoantibodies and destroying those platelets.

And in those patients who receive rituximab, whether it's failures or relapses on rituximab, you see this rich population of CD19-positive, CD20-negative plasmablast and

plasma cells that are driving disease. In fact, you actually can identify the autoantibodies being generated by those cells. And when you look at the populations, you can actually see that the CD19 cells proliferate and grow into the niche that's vacated by the CD20 cells when you give rituximab. And so we really know that they are the pathologic cause of ITP in those patients. And so by giving an anti-CD19 antibody, we hope to deplete that cell population and treat the disease.

We know in our experience in MN, but also the experience in NMOSD with inebilizumab, that CD19 does tend to work after CD20 in patients that fail CD20. So in their pivotal studies and even in real-world use, the inebilizumab is working essentially in all patients that fail CD20. And even in our MN study, we had one patient who had failed CD20 rituximab who received budiprotug, our drug, and had a complete remission of disease. So, taken together, you know, we know B cell depletion works. We know it typically works even after CD20, and then we have the identified biopsies that show these cells are secreting autoantibody. That leads us to a pretty strong argument CD19 is gonna work well, in fact, better than CD20 in this indication.

Yasmeen: And what do you hope to see in safety and tolerability and to warn moving forward into a phase 3 study and across your phase 2?

Aoife: I think our safety and tolerability is likely to look very similar to Laughlin's data. And there's nothing I think that would concern us based on what we've seen from the placebo-controlled study. I think theoretically there was a concern about an imbalance in infection risk based on the fact that B cells are an important component of the immune system, and we're essentially depleting B cells. When you look at all of the B cell-depleting therapies, the infection risk really increases when you're depleting the long-lived plasma cells that are really responsible for protective immunity, preventing you from getting infection that you've already been exposed to, right?

So things like BCMA, CD38, to deplete those plasma cells, tend to be the targets that increase risk of infection. If you look at all of the placebo-controlled data that's been generated with CD19 depletion, you see that there's very little imbalance in the risk of infection in the active and the placebo arm, but, obviously, that's gonna be something that we'll continue to watch as we develop the programs. The other thing that I think is less of a concern is going to be injection site reactions and fusion reactions where the

experience is very similar to rituximab. We will premedicate with paracetamol, antihistamines, but that's something that we'll look for, and we haven't seen any in the PMN data to date, but, obviously, that's something that we'll be monitoring for as we continue with development. And those are really the two things that, you know, I think are pertinent. Obviously, there's unknown unknowns that can come up in any development program, but those I think are the things that kind of prospectively come to mind if you think about initiating clinical trials with this modality.

Bill: Sorry. In terms of efficacy, you know, there's a base case kind of minimal efficacy that you wanna see, which is around 20% of patients, but we are ambitious here. We do think we can surpass the efficacy shown by rituximab and put up numbers similar to we have in MN, which is beyond the 50%, maybe the 60% to 70%. That's aspirational, but given the mechanism is well described and the drug should complete those cell types, we think it is achievable. So, yeah. I mean, we'll find out.

Yasmeen: Okay. And team, we'd love to also... So as you're gonna be running open label study, at what point do you wanna, like, come back to the market and communicate sort of update around it? Have you thought through that? Yeah.

Aoife: Yes. Yeah. I think we don't want to be dribbling out case studies. I think there's a lot of investor fatigue around that kind of approach. I do think it will be in the context of a presentation at an academic meeting where we can provide a full disclosure around all of the data, safety, the efficacy, the full thing. And I think it will be when we have a meaningful collection of data where we feel like there's something that can be interpreted and deduced. So I think that's gonna be our approach for a disclosure perspective.

Yasmeen: And then team, let's maybe spend a few minutes on SLE. Right? Maybe the first place to start off is, like, maybe educate us, what is the differentiation of CD19 versus CD20 and SLE in your view? That's sort of one. And then why run an open-label study versus more a placebo-controlled study in there? Would love to get your rational thoughts there.

Aoife: Yeah, for sure. So we know that B cell depletion works. B cell targets have worked in SLE, right? So we know that there are multiple B cell targets, whether it's CD40 live band or in others, they work. And I think what we've seen is the more potent your inhibition or your depletion of B cells, the more activity that you get. There's generally a linear

relationship between the extent of B cell kind of inhibition or depletion and the extent of the activity. So I think given the fact that we're going to deplete a broad subset of B cells, I think there's good biological rationale to say that we have potential to get better efficacy compared to bulimia, for instance, in others.

So I think we're optimistic based on the underlying biology and the precedent here that we can do something meaningful for patients with SLE. I think the real question we want to answer with our early field study and the reason that we're doing an open-label study is it's very similar to studies that are done with all of the other modalities that are evaluating SLE. We're starting off in patients with severe lupus. We're going to start at a low dose, look at their biomarkers, evaluate whether or not when we're depleting these B cells and the B cells are coming back, are they coming back in a new phenotype? What are we seeing in terms of the biomarkers of immune function in these patients.

I think that's really going to allow us to understand how we design the next placebo-controlled studies, because once you initiate a placebo-controlled study, you're kind of locked in. So you have to understand how we're going to dose this. Is it going to be chronic dosing? Are we going to attempt an immune reset with a high dose of an antibody? And those I think are questions we need to answer with this first study up front. So I think it's going to generate some really interesting data that will help guide a better design of a future placebo-controlled trial in SLE.

Yasmeen: Are the doses that you're selecting across these three indications the same or different? How do we think about them?

Aoife: They will be different. For instance, in PMN, there is potential that we'll see lower exposure just based on the fact that these patients will have proteinuria at baseline. As you know from other monotone antibodies, you can see protein leakage, so you get a little bit lower exposure in patients with high proteinuria levels at baseline. So there's potential that there may be differences in dosing across indications. So that's something that we need to evaluate as part of these initial programs.

Yasmeen: As you guys are going to be really doing a lot of the heavy lifting on starting the studies, is there other CD19 readouts in these indications or other indications that could serve as an inflection point for the doc in 2025? Yeah.

Bill: Yeah. In terms of antibodies, inebilizumab is another anti-CD19 monoclonal antibody. That is being developed in systemic sclerosis in Japan with the Japanese partner of Amgen, in that case Mitsubishi Tanabe. They still have phase 3 data, we believe, in some time in the middle of 2025. Of course, there are a number of other CD19 that are in modalities, the TCEs, the CAR-Ts, that will continue to generate data. In terms of real, you know, data sets, they are doing kind of patient by patient. The only kind of real data set in 2025 may be the T cell engager from ITabMed that is potentially in late 2025 in SLE. But other than that, you know, it's just these little dribs and drabs of data from the CAR-Ts and the other T cell engagers like Cullinan and others. So really the inebilizumab is the big...the SSC data is the big readout in 2025.

Yasmeen: Okay. Great. And then the recent cash that you guys rated in concurring with the pipe, where does it position you in terms of runway?

Aoife: So we had $218 million at the end of Q3, so well-financed and we're financed through 2027.

Yasmeen: Perfect. All righty.

Aoife: Great.

Yasmeen: Thank you so much for a great discussion and thank you again for being at our conference.

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