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EDITED TRANSCRIPT

Biomea Fusion Inc ADA Scientific Sessions Discussion

EVENT DATE/TIME: JUNE 27, 2023 / 12:30AM GMT

CORPORATE PARTICIPANTS

Ramses Erdtmann *Biomea Fusion - COO, President and Co-Founder*
Tom Butler *Biomea Fusion - CEO, Chairman and Co-Founder*
Steve Morris *Biomea Fusion - CMO*
Juan Pablo Frias *Biomea Fusion - Board of Director*
Rohit Kulkarni *Biomea Fusion - Board of Director*
Jose Rodriguez *Southwestern General Healthcare Center in Fort Lauderdale - Medical Director and Principal Investigator*

CONFERENCE CALL PARTICIPANTS

Yigal Nochomovitz *Citi - Analyst*
Eric Joseph *JPMorgan - Analyst*
Joe Cantanzaro *Piper Sandler - Analyst*
Peter Lawson *Barclays - Analyst*
Hartaj Singh *Oppenheimer - Analyst*
Tony Butler *EF Hutton - Analyst*
Eun Yang *Jeffries & Company - Analyst*

PRESENTATION

Operator

Good morning ladies and gentlemen, thank you for standing by, and welcome to Investor Conference Call and Webcast to discuss Biomea Fusion ADA Scientific Sessions presentation from San Diego. At this time, all participants are in a listen-only mode. After the speaker's presentation, there will be a question and answer session. (Operator Instructions) Please note that today's conference is being recorded.

I will now hand the conference over to your speaker host, Mr. Ramses Erdtmann, please go ahead, sir.

Ramses Erdtmann ***Biomea Fusion - COO, President and Co-Founder***

Yes. Thank you, Lyvia. Good morning everyone, and thank you for dialing in at this early hour. We're very excited to discuss with you this morning the press release we issued this past Friday evening, announcing data we presented at the American Diabetes Association's Scientific Sessions here in San Diego.

Some quick introductions from my side. My name is Ramses Erdtmann, I'm COO, President and Co-founder of Biomea. With me on the call today from our team and available to answer questions are our CEO and Chairman Tom Butler, also Co-founder of Biomea, as well as our CMO, Dr. Steve Morris.

Additionally, we are very fortunate and thankful to have joining us on this call today three renowned leaders in diabetes research and patient care, Dr. Juan Pablo Frias, Dr. Rohit Kulkarni, and Dr. Jose Rodriguez. Dr. Frias is the medical director and principal investigator at Velocity Clinical Research, headquartered in Durham, North Carolina, with more than 80 sites in the U.S. and Europe.

Dr. Frias is a former clinical assistant professor of Medicine Division of Endocrinology at the University of California, San Diego School of Medicine and former CMO and senior vice president of Clinical and Medical Affairs Diabetes Care at Johnson & Johnson.

Dr. Kulkarni is a senior investigator and professor of medicine at Harvard Medical School and has been a faculty member of the Joslin Diabetes Center since 1999. Dr. Kulkarni's laboratory primarily focuses on the generation of beta cells, which are the insulin producing cells that are primarily affected in type 1 and type 2 diabetes. Both Dr. Frias and Kulkarni are members of Biomea Scientific Advisory Board.

Dr. Rodriguez is a medical director and principal investigator at the Southwestern General Healthcare Center in Fort Lauderdale, and he has dosed several diabetes patients in our clinical study COVALENT-111.

Before we start, let me remind you that this non-confidential presentation contains forward-looking statements about the business prospects of Biomea Fusion, including expectations regarding Biomea Fusion's ongoing and planned regulatory and clinical

development activities, and trial results and potential future product candidates in different areas of therapeutic research and development.

Results may differ materially from those expressed or implied in this presentation depending on the progress of Biomea Fusion's preclinical and clinical development activities, actions of regulatory authorities, availability of capital, future actions in the pharmaceutical market and development by competitors, and those factors detailed in Biomea Fusion's filings with the SEC such as 10-Q, 10-K and 8-K reports.

All forward-looking statements made during this presentation are based on the beliefs of Biomea Fusion as of this date only, and future events or simply the passage of time may cause these beliefs to change. Please be aware that you should not place under reliance on these forward-looking statements made today.

We have uploaded a slide deck containing the poster presentation from this past weekend in the Events section of Biomea's IR website. Please refer to those slides during our prepared remarks.

I will now turn the call over to our CEO, Tom Butler. Tom?

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Thank you, Ramses, and thank you all for dialing in.

Last month, the FDA published new guidance for diabetes to help facilitate new therapies, and the FDA quoted the need for more antidiabetic treatment is clear. It's very fitting that the opening symposium at the 83rd, 88th annual meeting was titled, "The Pathway to Stopping Diabetes". We are all aligned with that mission.

And during that symposium, there were three presenters, all presenting very different ideas in how to stop diabetes. We feel that with BMF-219, we are well on that pathway. On Saturday, we presented groundbreaking data, lasting and improving responses in diabetes patients were observed two months after the treatment with BMF-219 had stopped.

In the dose escalation portion of the phase 2 study, diabetes patients received BMF-219 once a day for four weeks. After eight weeks of follow up, about half of the patients in Cohort 3, the higher exposure group, not only continued to experience their responses from BMF-219, but further approved upon them.

In other words, half of the patients improved their responses while being off treatment. With our first dose level 100 milligrams and first dosing duration testing only four weeks, which we feel is a very encouraging result. COVALENT-111 is the first trial in history that is enrolling type 2 diabetics treating for only four weeks, with the expectation that in some patients, not only will glucose control remain stable, glucose levels will actually improve over time after discontinuation of therapy.

And while we anticipate expanding the study to those patients with longer treatment periods of time on the order of eight to 12 weeks, this is truly a paradigm shift in the way we are studying the treatment of diabetes. You may recall that this trial, COVALENT-111, has very few restrictions in enrollment. Given the considerable heterogeneity of type 2 diabetes, we want to ensure we are capturing a real world understanding of BMF-219's impact across a broad spectrum of patient profiles.

In the Cohort 3 high responder patients, we also observed an increase in C-peptide production. C-peptide is created when the hormone insulin is produced and released into the body. So we can measure C-peptide levels to determine if the pancreas is producing insulin. C-peptide improved for these patients versus baseline, also, while they were off therapy.

The increase in C-peptide and the resulting improvement in HOMA-beta is unprecedented. Both maintained while off treatment for Cohort 3. Even though these are very small numbers, we believe they provide early clinical support for the proposed mechanism of action for BMF-219. Through specific disruption of the menin pathway, we believe we can improve the health and function of the islets by proliferating, reactivating, and preserving beta cells, which are the cells in the pancreas responsible for insulin production.

We believe that if a patient has a restored pool of healthy functional beta cells, the patient's own body then may be able to produce insulin and maintain glycemic control. Typically, once a patient has become diabetic, their healthcare provider is targeting a reduced elevated levels of A1c back to the range of 7% or below. At this level, the potential organ damage can be better controlled.

At week 12 in our study or eight weeks after the last dose of BMF-219, we observed this range for 60% of the patients in Cohort 3. It's important to note that none of the patients in Cohort 3 were at that target baseline of [7%] or below when we began dosing. The top 50% of responders or half the patient cohort in our study did particularly well while being off therapy. And the group demonstrated ongoing and durable reduction in hemoglobin A1c.

A continued reduction in hemoglobin A1c by an additional 114% was observed in Cohort 2. An additional 62% in Cohort 3 while being off treatment for eight weeks. Also of note, 70% of Cohort 3 patients maintained or improved their time in normal glucose range while being off treatment. Again, I'll just emphasize, we are seeing these continued and improved A1c reductions while patients are off therapy.

We believe this may be a new benchmark of success for an antidiabetic agent. We believe we are developing the first therapeutic agent for diabetes that has the potential to challenge the current paradigm of the approved agent's chronic dosing.

Within the next month, we will be testing additional dose levels and later in 2024, we will also be studying additional dosing durations. We believe we will then understand the full potential impact that BMF-219 may have on the various profiles of diabetes patients at various stages of their disease progression. We also intend to greatly increase the number of patients evaluated to gain further understanding of these initial observations.

As we review the COVALENT-111 results and assess the impact BMF-219 may have on beta cell function while off treatment, we feel it is too early to talk about potential long-term durability and the rate of beta cell proliferation. With these data, we have shown early clinical support of the proposed mechanism of action. We have observed that BMF-219 elicited an extended impact for some diabetes patients after short period, dosing period.

With glycemic control being maintained while off therapy and in many patients, the responses are even improved over time, which we believe and suggest that the pool of beta cells may have proliferated, reactivated, and the cells are seemingly healthier. And even though we see these as landmark findings, we are just getting started with our clinical development, BMF-219.

I will now turn the call over to our scientific advisers who will provide a bit more background on the diabetes landscape and our proposed mechanism of action. Juan?

Juan Pablo Frias ***Biomea Fusion - Board of Director***

Thank you, Tom.

Let me start by congratulating the Biomea team for achieving these unprecedented and remarkable results. I've been taking care of patients with diabetes all of my professional career, and I have not treated a single patient for a short period and seen improved results while off therapy. In fact, it's quite the opposite.

Patients frequently ask, as soon as they're diagnosed and therapy is initiated. Doc, for how long will I need to take these diabetes medications? And unfortunately, my answer today for all standard of care agents is more than likely for the rest of your life. I'm very excited that Biomea is exploring a new pathway to address diabetes and developing a potential solution to address a root cause of the disease, the depleted pool of healthy functioning beta cells.

Without healthy functioning beta cells, it is not possible to produce and secrete the insulin that's required to metabolize glucose in the bloodstream and to avoid high blood glucose concentrations, which not only define diabetes, but which can lead to important short and long-term complications.

As healthcare providers, we have many new and powerful agents available today, resulting in weight loss and other important benefits for our patients with diabetes. So you may ask, do we really need another medication in our arsenal? And the answer is a resounding yes, because, unfortunately, none of our past or new novel antihyperglycemic agents address the root cause of the disease.

This has been a major problem for the management of diabetes. Even while on standard of care therapy, beta cell mass and function will generally continue to deteriorate, with many patients losing this natural machinery, the beta cells, to the point where they become insulin dependent, requiring injected insulin to attain and to maintain adequate glycemic control.

The statistics surrounding diabetes in America today are grim. FDA recognizes this as well. On May 25th of this year, FDA published an updated draft guidance for the industry in which Deputy Director Lisa Yanoff from FDA Center for Drug Evaluation and Research remarked the following, and I quote, "Diabetes is a common disease that affects nearly 40 million people in the United States and is projected to affect more in the coming years. The need for more antidiabetic treatment options is clear."

Approximately one-third of these patients with diabetes are dependent on insulin injections. And more importantly, it's estimated that patients with diabetes lose, on average, 10 years of their lives directly due to the disease. Even though we have many approved therapies today, there is still an important unmet need in our current treatment paradigm.

Biomea, with its investigational BMF-219, offers hope not only here in the United States, but also worldwide. Today, the number of patients from the COVALENT-111 study are still very small, yet these data are quite encouraging, as patients have demonstrated very promising glycemic control while off therapy, which could be an indication that their pool of beta cells have repopulated and are producing insulin.

Many more patients at various dose levels and dosing durations of BMF-219 will need to be enrolled in the trial to fully explore its potential. However, if the current results are replicated, expanded and further supported, BMF-219 could become an impactful addition to today's diabetes treatment landscape.

I will now turn the call over to my colleague, Professor Rohit Kulkarni.

Rohit Kulkarni ***Biomea Fusion - Board of Director***

Thank you, Juan. And allow me to start by also congratulating the team at Biomea.

I've been studying beta cell health for more than 30 years and have not seen human data quite like these before. Let me provide some background about how diabetes develops. When people are on the path to developing diabetes, they generally begin to lose functional beta cells, and as a result, they are not able to secrete enough insulin to maintain glycemia.

The beta cells are thought to be depleted because they're dying, they're unable to regenerate or replicate or all of the above. These patients also develop insulin resistance, which means glucose is not being taken up by the tissues, such as the liver, skeletal muscles and fat and so forth. This can lead to higher glucose levels and eventually to develop over type 2 diabetes.

Beta cells play a very critical role because they have to keep secreting functional insulin to maintain appropriate glucose levels. Also of note, beta cells in humans have been estimated to last a very long time and not replicate very often. They reach their maximum levels by about 10 to 20 years of age, so losing them or having them depleted is quite consequential.

Now, patients with type 2 diabetes over the years have been looked at much more carefully, and recent data tells us that not all patients with type 2 diabetes have the same kind of pathogenic processes. It's becoming clear now that some individuals have extremely severe insulin resistance, even though their beta cells are functioning well.

On the other hand, there are other subsets of type 2 diabetes where there appears to be a deficiency of the beta cell pool and these cells are unable to replicate. As the disease progresses, there may be a relative loss of functional beta cell mass. This is a very important finding, and one which is not appropriately addressed by any of the currently approved therapies for type 2 diabetes.

Looking at these early BMF-219 data presented at the ADA, it appears that BMF-219 could potentially have a comparatively greater impact in those individuals who have a failure of their beta cells, individuals who are poorly replicating beta cells or beta cells which are deficient, or even beta cells which have not been reactivated.

On the other hand, treating individuals with BMF-219 that are primarily insulin resistant might not show much of a change because those individuals might already have a sufficient number of beta cells. The improvement in C-peptide levels for the responder patients is really exciting.

Currently, the treatments for type 2 diabetes are geared towards maintaining glucose levels within the normal range, and so all the treatment modalities have generally been geared towards this component. Today we have many agents that are improving insulin sensitivity. However, we are lacking agents that restore the pool of functional beta cells which improve their health and function.

There is no therapeutic agent today that is known to address the depleted pool of functional beta cells. Ultimately, we have to think about how we may be able to cure patients with this disease. And it's logical to assume that curing the disease is reliant on addressing a root cause of the disease, which is deficiency of beta cells, beta cells which are not regenerating or reactivating and not functioning appropriately.

As an agent specifically designed to improve beta cell function, I'm very encouraged by BMF-219's development progress and I believe BMF-219 could play a very important role in the treatment of this disease.

I will now turn the call over to Dr. Jose Rodriguez and investigator in the COVALENT-111 study.

Jose Rodriguez ***Southwestern General Healthcare Center in Fort Lauderdale - Medical Director and Principal Investigator***

Thank you Professor Rohit, and thank you to the Biomea team for inviting to participate in this conference call to share some of our clinical experiences with you.

In our clinic, we are primarily conducting human clinical studies enrolling patients with type 1 and type 2 diabetes. Most of our patients are from Hispanic background and many of them are overweight and have elevate A1c levels at the time of diagnosis. They often have other comorbidities, including hypertension, hyperlipidemia and many other chronic conditions associated with diabetes.

Unless there is a contraindication, we start the patients who are above an A1c of 8% of an oral agent, typically metformin, a second line of therapy we use we often use sulfonylureas as they are inexpensive. We adjust the agents based on the patient's particular health profile.

In our treatment plan, we also take in consideration that many of our patients don't like injectables and prefer oral agents. Each patient receives a personalized treatment plan based on their particular health situation, their risk factors non-comorbidities, their medication and diet complaints, and their response to treatment. We often need to make adjustment as treatment fail or side effects arise.

As Dr. Juan mentioned, a primary concern of patients is the duration of treatment. How long will they have to take their medication? And of course, without lifestyle changes, the duration of therapy is often for life. As patients entering our clinic, they might have diabetes for a prolonged time without knowing this complicated issue. As all we might be able to do their needs, we work with an already depleted pool of beta cells. Their advanced status may be more severe than initially assumed.

With respect to COVALENT-111, the following is a summary of our experiences to date. For the enrollment criteria, patients enter the study with high levels of A1c between seven and 10. Their glucose levels are uncontrolled, meaning their standard of care medication is currently not working for them.

In our center, for those patients we have dosed, they felt very good from the start. Their A1c had dropped in some cases even drastically. For example, I have one patient with a baseline A1c level of around 9.5, and after four weeks of treatment, the A1c had dropped to 7.8.

For the clinician's perspective, these are very encouraging data, which becomes even more exciting, is such a decrease matches with the way the patient is feeling while on the study. Their subjective symptoms. So far, the patients we have dose in COVALENT-111 typically reported they are feeling really good.

We use many agents in our clinic that are associated with a spectrum of side effects for patients like hypoglycemia, GI symptoms such as diarrhea, bloating, loss of appetite, et cetera. So far, we have not really seen any of these side effects. BMF-219 has been generally well tolerating this study either on or off therapy.

One thing we are particularly afraid of in treating any of our patients is the increase in A1c after it has dropped. If an agent is capable to lowering A1c from 7.5 to 6.9 and we keep it there, while it doesn't seem like a significant change, we are really happy with such results. We want to keep these levels stable and avoid A1c to go meaningfully higher.

So far, we have been very encouraged with the early data from this study, and I continue to monitor the patients for five additional months while off therapy. Even with our small sample of patients, the best continuation of responses we observed so far were individuals who improved the A1c numbers, even further while being off therapy.

So far, BMF-219 in our clinic has led to encouraging patient enthusiasm -- an enthusiasm I share as well.

Thank you. And now we turn the call over to Biomea Chief Medical Officer, Dr. Steve Morris.

Steve Morris ***Biomea Fusion - CMO***

Thank you, Jose, and to our scientific advisers for the important context they provided. We shared the poster on Saturday with you and also presented a comprehensive slide deck of the patient results after treating only 20 patients with BMF-219.

The initial response of BMF-219 impacting diabetes in general has been very impressive. In particular, the number of patients treated with BMF-219 who showed an improvement in A1c since we initiated the study, especially those patients who achieved the goal of reducing their A1c to the target level of 7% or below. That number now, after four weeks on therapy and eight weeks off therapy in our Cohort 3 patients is at 60%.

We are also encouraged by C-peptide numbers which reflect increased endogenous insulin secretion. Here we observe C-peptide levels to improve and to correspond with the A1c reductions. I'll just echo what our previous speakers noted. As a treating physician, I have not seen an agent providing such data while a patient is off therapy.

As Dr. Kulkarni explained, beta cells are long lived, so we now have to see how these patients will do over time going forward. During our study so far, we have not observed any symptomatic hypoglycemia or any weight gain, and BMF-219 has been generally well tolerated, as Dr. Rodriguez described. And our safety and tolerability slide showed in our March data deck.

We continue to explore BMF-219 in a variety of different diabetes patient profiles, greater detail as the study continues. But what we've learned so far is that covalent inhibition of menin with BMF-219 seems to have an initial important impact on diabetes markers. We believe this strongly supports our hypothesis that BMF-219 is a potential first in class covalent menin inhibitor with efficacy for a variety of patients with diabetes.

As of today, we've only completed two dose levels with sufficient follow up 100 milligrams daily fed and fasted, and only 20 patients altogether with just an initial dosing duration of four weeks. As Tom noted, we hope to significantly expand the number of patients dosed over the coming quarters.

We recently completed dosing patients with the 200 milligram fasted cohort, which is now in the follow-up period. The 200 milligram fed cohort led to an increase in mild to moderate nausea compared to 200 milligram fasted. So this cohort will be transitioned to [100 milligram] BID dosing.

No other clinical symptoms, clinical concerns observed at this dose level. Coming months, we also intend to test and improve BMF-219 formulation designed to reduce the variability of food effect. We plan to take this new tablet into the expansion phase next year.

As Tom indicated in his opening remarks, we will continue our enrollment, identify the optimal dose level and also the length of dosing best suited for the largest patient pool in order to fully explore the characteristics of BMF-219 and define the optimal patient profiles of those individuals who experienced the most significant benefits from this important therapy.

I will now open the floor for questions.

QUESTIONS AND ANSWERS

Operator

Thank you. (Operator Instructions) Now, first question coming from the line of Yigal Nochomovitz with Citi. Your line is open.

Yigal Nochomovitz ***Citi - Analyst***

Yes, hi. Thank you very much for taking the question. For the three KOLs on the line, if you could answer the following. It's a very simple question, but obviously with profound implications potentially for the mechanism.

Is there anything else besides beta cell proliferation? Some people pointed to diet and exercise that could possibly explain the maintenance of this response on HbA1C and C-peptide and HOMA-B that is occurring beyond -- two months beyond the last dose. And then secondly, with patients on any background therapy, and was there any type of rescue protocol that was used at all in this study or no? Thank you.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Juan, do you want to take this?

Juan Pablo Frias ***Biomea Fusion - Board of Director***

Yes, no, no, absolutely. Thank you. Yes. So to the first point, whether there was anything else that could explain this, in that short period of time, I would say no, it would be extremely unusual. I mean, this is a relatively short period.

So, and there are no real changes in body weight. My understanding in the protocol is that there's no lifestyle intervention that's done as well with this. So I would say, no, there's nothing else really to explain this or will be a feasible explanation for the reduction and the improvement in glucose.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Rohit?

Rohit Kulkarni ***Biomea Fusion - Board of Director***

No.

Jose Rodriguez ***Southwestern General Healthcare Center in Fort Lauderdale - Medical Director and Principal Investigator***

Right. So the medication that you usually use is only metformin. And so we haven't seen any hypoglycemia -- symptomatic hypoglycemia events in any of our patients already dosed with the BMF-219, no. No symptomatic hypoglycemia.

Yigal Nochomovitz ***Citi - Analyst***

Okay. And then with regard to the C-peptide data, which the company showed, can you just talk a little bit more detail about whether that how that data squares with you? Does it make sense in terms of seeing the lower baseline C-peptide and the higher rise in C-peptide in the patients that benefited the most on HbA1C versus the patients that benefited less on HbA1c that started with a higher baseline C-peptide and had a lower C-peptide response? Thank you.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Rohit?

Rohit Kulkarni ***Biomea Fusion - Board of Director***

Yes. So I think -- so the alterations in C-peptide levels would be a direct reflection of the number of beta cells which are either being reactivated or potentially getting healthier, although we don't expect the regeneration or replication to occur so early. So the change in C-peptide in different individuals would reflect the different pools of reactivated beta cells.

So individuals with higher HbA1c could have a larger pool of sleeping cells which could be reactivated and vice versa. If the HbA1c is low, that pool may be smaller, so the response is appropriately smaller. So these changes in C-peptide potentially reflect different pools of reactivated beta cells.

Yigal Nochomovitz ***Citi - Analyst***

Okay. Thank you.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

And Yigal, I just want to make sure we answer your question about the rescue therapy and what else could explain the continuation of the decline in A1c. There was rescue therapy for only one patient in the study, and that was a placebo patient in Cohort 2. That's the patient shown at least 0.5% reduction in A1c.

Yigal Nochomovitz ***Citi - Analyst***

Okay, got it. Thank you.

Operator

Thank you. One moment for our next question now.

Now next question coming from the line of Eric Joseph with JPMorgan. Your line is open.

Eric Joseph ***JPMorgan - Analyst***

Hi, good morning. Thanks for taking the questions and fairly incorrect on these results. I guess just a housekeeping question as it relates to some of the data presented here, particularly on C-peptide as it relates to responders.

I guess from the company, can you just kind of detail at baseline, there are sort of some low sample numbers at baseline, I guess, what kind of accounts for maybe missing data capture there and your confidence level, and that the trend in rising C-peptide over time is an accurate reflection. And...

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Happy to answer Eric. Steve, you want to take it?

Steve Morris ***Biomea Fusion - CMO***

Sure. I'm happy to address that. So for some of the subjects in Cohort 3, unfortunately, we had mishandling of the baseline samples, so we're lacking data for some of those baseline C-peptide results. However, I'll point out that we do have the remainder of the time points C-peptides for those time points.

And you'll know that we see a substantive increase, for example, from week two, the C-peptide determinations at week two relative to the time points after week two. That's the reason why there's a relative paucity of time points at baseline.

Eric Joseph ***JPMorgan - Analyst***

I see. Thanks. And then sorry for the feedback here, but I guess as it relates to this tolerability issue that you observed at 200 milligrams with food, I guess the thinking previously was that administration with food kind of had a negative impact on overall exposure. That

being said, you didn't see a tolerability issue in the 200 milligram without food, which is kind of counter to that, I guess, expectation, right?

So I guess what, in your view, or maybe from the -- in the view of your KOL guests might be driving some of that tolerability challenge with food administration. And then I'm also curious to know whether there are any early signs of further dose response for the 200 milligram without food that you've observed so far. Thank you.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Yes, absolutely. Happy to take that first. This is Tom, and then I'll pass it on to Juan and Dr. Rodriguez. With the 200, it's kind of interesting and we don't know, right, is this just related to the effects of patients taking the drug with food, have high blood sugar. We've looked at these exposures, obviously, the same exposures. We don't see this happening when there's not food.

And then also, in our experience with the oncology trials, we're in much higher concentrations or exposures where we don't see this. So it looks to be related to having with food and having high blood sugar. And Juan?

Juan Pablo Frias ***Biomea Fusion - Board of Director***

Yes, I think that would be the explanation for now. I think, again, these are very small numbers. We need to look at this further. And I would say, clearly, these are the types of side effects that we see with many of our anti-diabetic agents, but I'm not sure what the mechanism would be, and I think it's something that clearly needs to be explored further.

Eric Joseph ***JPMorgan - Analyst***

Okay, thank you. And just taught any early signs of dose responsiveness, I guess, for -- even though it's just sort of the on treatment phase with 200 milligram without food.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Sorry, I missed the beginning of your question.

Eric Joseph ***JPMorgan - Analyst***

For the 200 milligram without food.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Yes.

Eric Joseph ***JPMorgan - Analyst***

I know you're in the post-treatment follow up, but just for the first four-week on treatment phase, any signs of dose responsiveness worth discussing at this point or perhaps too early to tell?

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

We're still waiting to get all the data from the sites, so we'll be cranking that data through over the next few weeks.

Eric Joseph ***JPMorgan - Analyst***

Great. Thanks for taking the questions.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Of course. Thank you.

Operator

Thank you. One moment for our next question. And our next question coming from the line of Joe Cantanzaro with Piper Sandler. Your line is open.

Joe Cantanzaro *Piper Sandler - Analyst*

Hey, guys. Appreciate you taking my questions and congrats on these data here. Maybe first one for the KOLs on the call, it would be great to hear their thoughts around what's the first PD marker that they monitor or see change when a type 2 patient starts to lose benefit from a drug they were previously benefiting from.

And maybe somewhat relatedly if they could speak to what they would expect for CGM data for other type 2 therapies. And how quickly time and range decreases upon stopping those therapies? Is that something that's observed within a matter of days, weeks or months? Thanks. And I have a follow up after that.

Steve Morris *Biomea Fusion - CMO*

Juan, could you take that perhaps?

Juan Pablo Frias *Biomea Fusion - Board of Director*

Yes, no, absolutely. So, great question. And I think as far as the pharmacodynamic marker, generally, we're looking at A1c. So that clearly takes a longer time with almost any medication with respect to sort of getting a hint that you're losing control. But with continuous glucose monitoring, we're using it more and more. You would see that generally much quicker when you're just looking at time and range or mean glucose with the CGM.

And with respect to loss of efficacy when either you -- when you stop an agent, we generally don't stop agents, we add on top of agents. But I would say it's going to really depend on the half-life of the agent as well, whether it's the weekly agent, a daily agent.

But, generally, you would start seeing glucose coming up even with the GLP-1 receptor agonist or dual agonist within a couple of weeks, certainly by four weeks. And generally, when I'll see this in patients who have run out of medication or we've had an issue getting their medication, for example, and you see it relatively quickly, it's not something that takes a long time.

And oftentimes, patients will even contact us that they've missed a dose or two doses of a weekly medication and they're seeing their fasting glucose rising. So it could be something that the patient is seeing clearly, though CGM is the best thing and sort of a lagging indicator would be the A1c. But relatively quick loss of control when any of standard of care medications really are stopped in today's kind of with what we have available today, I would say.

Joe Cantanzaro *Piper Sandler - Analyst*

Okay, great, that's helpful. And then maybe a follow up one for maybe the company, I guess. Can you elaborate a little bit when you say there was no meaningful change in hemoglobin levels? I guess, what amount of hemoglobin changes defined as meaningful here? And did you look at any other markers of red blood cell changes, like reticulocytes or anything else? Thanks.

Tom Butler *Biomea Fusion - CEO, Chairman and Co-Founder*

Yes, I'll hand it over to Steve to take that. But no changes in hemoglobin A1c or red blood cell compartment, meaning, any changes that we saw would have an impact less than a 10th of a percent of A1c. And Steve?

Steve Morris *Biomea Fusion - CMO*

Yes, indeed, Tom is correct. And the reason for this question, for those of you who may not be aware, a trivial explanation for a reduction in A1c in response to treatment with a particular agent is if that agent might increase hemoglobin production.

If that were the case, in turn, that would reduce glycolated hemoglobin, i.e. hemoglobin A1c. But that reduction would have nothing to do with glycemic control. So that's the reason for the question. Again, as Tom mentioned, we've seen no increase or for that matter, decrease in hemoglobin in subjects dosed with 219.

The other thing I'll point out is that the reductions in A1c that we've observed with the subjects are totally consistent with the CGM data and the reduction in average glucose over time based on the CGM. So a direct correlation with that average glucose reduction and the A1c reduction. So everything is internally consistent.

Joe Cantanzaro ***Piper Sandler - Analyst***

Okay, great. Thanks so much. I appreciate you guys taking my questions here.

Steve Morris ***Biomea Fusion - CMO***

Thank you.

Operator

Thank you. And our next question coming from the line of Peter Lawson with Barclays. Your line is open.

Peter Lawson ***Barclays - Analyst***

Great. Thanks for taking the question.

Just your thoughts on the long-term exposure to menin inhibitor, even if it's potentially just for intermittent use and kind of anything you can triangulate from the (inaudible) AML patients would be great.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Sorry, Peter, you just broke up a little bit. Do you mind repeating the question?

Peter Lawson ***Barclays - Analyst***

Yes. Just your thoughts on the long-term exposure to a menin inhibitor for patients, even if it's for intermittent use and anything you can kind of triangulate from the menin inhibitor use over kind of a longer or extended period of time with your AML study.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Yes, absolutely. I mean, we have patients on our AML study out past six months, and the safety profile continues to perform extremely well. So we're very encouraged with long-term dosing of BMF-219. Our long-term toxicology studies back that up. And so we're excited to submit all this data to the FDA and then allow us to go into the expansion phase and dose up to 13 weeks.

Peter Lawson ***Barclays - Analyst***

Got you. And then just your thoughts around why the C-peptide starts returning to normal in Cohort 3. So that's one of the first figures from figure four. So that's page 13.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Yes, I think, obviously, we had the question from Eric about the baseline. Only one patient there. It's only one patient who had at least a 1% reduction. And even if you use week two as your baseline, the increase that we're seeing up to week four and beyond is extremely impressive.

And the resulting increase in HOMA-beta is unprecedented. It's easy. You can go back and look at PD effects of some of the approved incretin agents out there and compare appropriately with beta increase. Those incretins typically see an 80% to -- 85% increase in HOMO-beta. We're showing you approximately a 200% increase in HOMO-beta.

And that's really driven through the reduction in post and the increase in C-peptide. And it's very clear. The reason why you can see that reduction from week eight and beyond, I'll turnover to Rohit.

Rohit Kulkarni ***Biomea Fusion - Board of Director***

Yes. So that's a good question. I think it all relates to physiology and autoregulation, because as an example, when we have a meal, the C-peptide goes up in response to the glucose. And once the glucose starts coming down over a couple of hours, the C-peptide goes down.

So let's assume then you have a medication which is potentially reactivating beta cells, and initially, the glucose is high in these individuals. So the C-peptide is sustained for a longer period of time. But when the glucose starts getting back into in range back into the

normal component, then it begins to go down.

And so this is a very expected data in the context of the C-peptide coming down, because when the glucose is low, we don't anticipate the beta cell to respond at a high level. So, I hope that -- yes.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

That's exactly right. And keep in mind, we showed this in the CGM data, right, that Cohort 3 either maintains, but the majority actually improve their time in normal range. That means we're conducting the OGTT experiment. These patients are starting at a lower baseline, so they need less C-peptide, right, to control the insults of the OGTT experiment.

Peter Lawson ***Barclays - Analyst***

Got you. Thank you.

And then kind of -- there are some patients that when hypoglycemic kind of -- for how long did that happen? It was a short period of time, long period of time? Just any data around that would be great, shown in Figure 6.

Steve Morris ***Biomea Fusion - CMO***

Sure, I'm very happy to speak to that. So there were two subjects that had very transient, very mild hypoglycemia. And importantly, those subjects had very favorable responses to 219. Their time and range increased markedly. For example, one of those subjects had over 90% time in normal glucose range.

So the suggestion from that observation is that a subject with such a profound response actually probably should perhaps decrease or maybe discontinue their standard of care. Now, we have not yet allowed that in the clinical protocol, but we're discussing that possibility internally that we're reverting at least some subjects with 219 to a very favorable time and range. Perhaps, we start decreasing or actually discontinuing standard of care.

Peter Lawson ***Barclays - Analyst***

Great, thank you. And just a question for Juan and Jose just around any anecdotal evidence around safety. We didn't get kind of a deep dive around safety so I'm just curious any evidence you have around that safety profile for the patients.

Jose Rodriguez ***Southwestern General Healthcare Center in Fort Lauderdale - Medical Director and Principal Investigator***

So how are you? So, no -- this is Dr. Rodriguez. So I haven't seen any like a significant side effect. Like I said, the patient, they are doing really well. And you can see it's not only the numbers, you have to match the result of the number with how the patient, their feeling, like a subjective symptoms.

So they're feeling great. They don't have any side effects. Actually, sometime they doubt they are taking the medication because they -- like I said, there is no single one medication for standard of care diabetes that you can stop and continue having the good numbers matching with the symptom of a patient who's experiencing while taking the -- while off of therapy or while in therapy. So they are feeling really good. There is no concern about safety or any serious adverse event.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Thank you and thanks you for the question.

Peter Lawson ***Barclays - Analyst***

Thank you.

Operator

Thank you. And our next question coming from the line of Hartaj Singh with Oppenheimer. Your line is open.

Hartaj Singh ***Oppenheimer - Analyst***

Great, thank you. Thanks for -- and I got a couple of questions and really nice data. So congratulations to everyone there.

Just one is -- first question I have is you have kind of an interesting couple of just charts embedded in figure five where you mentioned that patients in Cohort 3 tend to be more recently diagnosed with type 2 diabetes. Can we make the assumption that if patients have a greater pool of beta cells, then you'd want to go earlier with BMF-219?

I know that's down the line because you want to preserve that beta cell functionality, go even maybe into prediabetes patients. I mean, is that a possibility? And then a follow up to that would be that if patients are not on background medications, meaning that they're earlier in their diabetes, for lack of a better term journey, then you could actually see a larger effect size with BMF-219 because they're less well controlled but have greater beta cell pool at that point. Thank you.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Yes, I'll hand it off to Rohit first to start.

Rohit Kulkarni ***Biomea Fusion - Board of Director***

Yes. So I think that's a good point. So in the context of what is the amount of beta cells available in the different individuals can be variable. I mean, even in healthy individuals, we know that there are pools of beta cells which are primed to regenerate potentially.

There are pools of beta cells which are potentially half asleep. So even healthy individuals, we know that we don't function maximally unless it is really required. So, for example, in pregnancy, you see that the traditional pool starts to be activated.

So in type 2 individuals, you can also imagine the heterogeneity of the individual pools. And therefore, if one were to anticipate a maximal effect from 219, I agree that having that compound in individuals who are starting with a low C-peptide could have a maximal effect.

But then over a period of time, I think it all depends upon how the beta cell is being recruited, right? And the activity pattern of the individual, what other medications he or she is on. So it could be available response in different individuals.

And then the second question about the prediabetes, yes, absolutely. I think that if you are able to identify those individuals who are already trying to decompensate at an early stage, we think that the 219 would have a greater impact at that stage in pretty much all individuals.

And I could also state that individuals with severe insulin resistance could also benefit in that context because the beta cell has not completely reached its maximum as compared to an individual with severe insulin resistant for a long period of time. So prediabetes would be a great target for 219.

Hartaj Singh ***Oppenheimer - Analyst***

Thanks, Rohit. And then just on the follow up that, let's say, if you had patients with lesser background medications or -- I know this is very hypothetical, but maybe not on background medications because they're earlier in being diagnosed as diabetes patients, then could we actually see a larger effect size because these patients are considerably less stable? Or that's just very early hypothesis or maybe not relevant? Thank you.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Yes, I think it's a good question, Hartaj. It's something that we have to sort out, and we certainly will do so when we get to larger patient numbers, and as we transition to the expansion phase. But the early signs that we see that the higher baseline A1c is generating a higher response, that's true for all antidiabetics, but it's even more true for 219 because we know that the proliferation rate of the beta cells when exposed to 219 is proportionate to the level of blood sugar for the patient.

So higher A1c means more blood sugar, which means more proliferation. And all it's saying is that, look, the four weeks of treatment, you

just have a higher probability of having a significant response that is maintained. And then certainly, as you are earlier in your progression of the disease, the background proliferation capacity is just higher. Hope that makes sense.

Hartaj Singh ***Oppenheimer - Analyst***

Yes. No, no, that helps a lot, Tom. Thank you for all the questions. And again, congratulations.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Thanks, Hartaj.

Operator

Thank you. And our next question coming from the line of Tony Butler with EF Hutton. Your line is open.

Tony Butler ***EF Hutton - Analyst***

Thanks very much. Thanks for taking the question.

There are two, and if I may, I'll recite both at the beginning. To follow on the last question about high levels of HbA1c and/or the time to have been diagnosed with diabetes being early, I wonder if, in fact, there's some information gathered based upon that data that actually supports or informs you for how to actually continue the expansion phase of the study.

So, for example, clearly a number of patients are going to be late in their diagnosis and or have low levels of HbA1c, what can you say mechanistically that might lead you to be informed of how a subsequent expansion might come together?

And second, Dr. Frias, you made a comment about supportive trials, trials that can replicate the existing data and, of course, expanded study. And I wondered if you had some information or some thoughts around what expanded populations you might want to see addressed and how they might be addressed with 219. Thanks very much.

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Thanks, Tony, for the questions. I'll take the first one and hand it off to Steve.

Steve Morris ***Biomea Fusion - CMO***

Sure. So, in terms of parameters that might allow us to benefit patients predicting their responsiveness to 219, as we have released in the -- this past weekend in our poster at ADA, the suggestion is that time since diagnosis may reflect responsiveness, that is the sooner after diagnosis, the greater the response.

Now, I emphasize the patient numbers are still very, very small, so we have to confirm that. But that is at least a suggestion. Another suggestion is that in terms of BMI, the leaner patients tended to have a more profound A1c reduction. Now BMI is, in large part, a surrogate for insulin resistance. So we'll be looking at BMI, we'll also be looking at insulin resistance.

And then finally, as it has already been mentioned, the higher the A1c at baseline, in general, again, the trend was to a greater reduction in A1c in response to 219. So those are three early parameters that suggest perhaps to be predictive of the magnitude of the response to 219. But again, to emphasize the numbers are small, we have to confirm these as we increase the total number of patients.

And then I think you had another question. Can you remind me of that question?

Tony Butler ***EF Hutton - Analyst***

Yes. One was, it was -- to Dr. Frias about comments he made with respect to expanded trials, certainly supportive studies. So the ones that were presented, the question is are there -- what types of populations might one -- might he suggest one would like to see to be supportive of the existing data? Are there any different types of patient populations that might be supportive? Thank you.

Juan Pablo Frias ***Biomea Fusion - Board of Director***

Yes, I think there are a couple of things. One with the dosing. So I think we need to figure out optimization of the dosing, both the dose and the duration of dosing. So that's one. With respect to patient populations, I think it's the populations we've been discussing, either early type 2 diabetes, so I would say at diagnosis, or at least within the first five years or so of diagnosis.

And then I think those patients with prediabetes that are sort of in that category where today we consider metformin A1c over 6%, maybe women who've had gestational diabetes, for example, there's very sort of at risk patients for converting to type 2 diabetes. So I think those early patients would be extremely important to look at.

Tony Butler ***EF Hutton - Analyst***

Thank you for the answers to the questions.

Operator

Thank you. And our next question coming from the line of Eun Yang with Jeffries. Your line is open.

Eun Yang ***Jeffries & Company - Analyst***

Thank you. Thank you for taking my questions. So, next step is to complete dose escalation and identify optimal dose. So with the 200 milligram QD, because of the GI issue, you are planning for 100 milligram BID. So the question is, by end of this year, when we see the data, would that be QD or BID dosing?

Tom Butler ***Biomea Fusion - CEO, Chairman and Co-Founder***

Yes, I think I'll pass onto Steve, but just real quick. So that's correct. We're conducting the 200 milligram without food and the 100 milligram BID without food. And we're doing the BID just so that we can see, is there a benefit to BID dosing with 219? When you look at our preclinical work, we -- in the ZDF animal model, we compared QD to BID.

It looked like there wasn't that much of an improvement, but we still wanted test this to see how it works in real life patients. But for us, 100 milligram has continued to perform extremely well. We want to see is it 200 mg without food or is it 100 BID without food? That would be the second dose. We'll push to two doses.

Steve?

Steve Morris ***Biomea Fusion - CMO***

The other thing I'll add to what Tom said is that to date, we've been dosing patients with a capsule formulation of BMF-219. Later this summer, we'll have a tablet formulation. And the plan when we begin the expansion portion of the study is to dose patients with that tablet formulation.

Now, the reason we think that's important is a tablet, unlike a capsule, will more reliably dissolve essentially spontaneously in the stomach. That's important because the bioavailability of 219 is dependent in part on PH. The lower the PH, in general, the better the bioavailability.

So, if a capsule fails to dissolve in the stomach, if it goes into the small intestine where the PHs is much higher, we take a hit on bioavailability. So again, we think that issue will largely, if not, completely be resolved with a tablet formulation as well as some of the negative food effect that we've reported with the capsule formulation.

Eun Yang ***Jeffries & Company - Analyst***

But the tablet formulation you're going to be using in next year, correct? Not in two times daily BID dosing.

Steve Morris ***Biomea Fusion - CMO***

That's correct. It'll remain in the capsule? That's correct.

Eun Yang *Jeffries & Company - Analyst*

Okay. And then another question is initially, you were looking at 100 or 200 or 400 or 600 milligram dosing. And can you talk about where are you in dosing? Is there 400 or just a completed 200? That's the first question.

And second question is that you guys mentioned that you would identify optimal dose by end of this year. Does that mean you are not going pushing the dose higher beyond 200 or 400? Thank you.

Tom Butler *Biomea Fusion - CEO, Chairman and Co-Founder*

Yes, great question. So TBD, what we'll do is we'll look at the data from the 200 and 100 BID. We'll evaluate the four week and follow up data. If it matches our expectations, then we'll move those two dose groups into the expansion. If we feel that there's still more efficacy on the table and safety allows us to do it, we'll escalate to 400 and 600 accordingly.

So we can go up to 600 and certainly without food shouldn't have a problem. So it's available if we need to. It's just that with the results of the 100, to be honest, it's unlikely you would have to go to 400 to 600, right, to form as the 100 has done.

Eun Yang *Jeffries & Company - Analyst*

Okay, thank you.

Tom Butler *Biomea Fusion - CEO, Chairman and Co-Founder*

Okay.

Operator

Thank you. Ladies and gentlemen, and we are getting past the one-hour mark. I will now turn the call back over to Biomea Fusion CEO, Mr. Tom Butler for any closing remarks.

Tom Butler *Biomea Fusion - CEO, Chairman and Co-Founder*

Great, thank you very much.

At Biomea, we aim to bring diabetic patients back to a normal, healthy state of glycemic control as effectively, safely and naturally as possible. With our COVALENT-111 study, we seek to establish BMF-219's potential ability to regenerate, preserve and reactivate healthy, functional, insulin producing beta cells.

And in doing so, potentially deliver the first disease modifying treatment for diabetes, a therapeutic solution that tens of millions of patients in the U.S. and over a half a billion patients globally need and deserve.

With these data, we have made important progress in understanding BMF-219's potential impact on beta cells and the underlying proposed mechanism of action of covalently inhibiting menin. We are eagerly to deepen our understanding of the potential reach of this investigational oral agent. And as a monotherapy or combination in type 2 diabetes and possibly in type 1 as well.

In closing, I want to thank Team Fusion for achieving this incredible milestone while pushing all of our other programs forward. My teammates here are incredible professionals. They're executing at the highest level of scientific excellence.

When we started Biomea, we defined our mission as we aim to cure. Being able to address diabetes at its root cause, impaired beta cell health, mass and function is an ideal manifestation of that mission.

Thank you for your interest in our developments and for dialing in so early. Have a great day.

Operator

Ladies and gentlemen, that does conclude our conference for today. Thank you for your participation. You may now disconnect.