BIOMEA Fusion's FDA Clearance of IND for BMF-219 in Type 2 Diabetes Conference Call Transcript provided by NOTIFIED

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- Dr. Rohit Kulkarni; Biomea Fusion, Inc.; Member of the Biomea Scientific Advisory Board

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- Eric Joseph; JP Morgan; Equity Research Analyst
- Michael King; EF Hutton; Managing Director and Head of Healthcare Research
- Eun Yang; Jefferies & Company; Analyst
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PRESENTATION

Operator: Good day and thank you for standing by. Welcome to the FDA clearance of IND for BMF-219 in type 2 diabetes conference call.

At this time, all participants are on a listen-only mode. After the speakers' presentation, there will be a question and answer session. To ask a question during the session, you will need to press star 11 on your telephone. Please be advised that today's conference is being recorded. I would now like to hand the conference over to your speaker today, Ramses Erdtmann, President of Biomea Fusion. Please go ahead.

Ramses Erdtmann: Thank you, operator. Good afternoon, everyone, and thank you for dialing in. My name is Ramses Erdtmann. I'm the 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, our Senior Medical Director, Dr. Sanchita Mourya, and our Associate Director of Translational Research, Dr. Priyanka Somanath.

Additionally, we have Professor Rohit Kulkarni on the call. Dr. Kulkarni is a member of the Biomea Scientific Advisory Board, currently 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 investigates beta cells, which are the insulin producing cells that are affected in type 1 and type 2 diabetes. Dr. Kulkarni will only be available for his prepared remarks. He's, unfortunately, traveling today for the remainder of the call.

Some of you may have questions related to our oncology trials; please call us directly with those. Today, we're solely focused on BMF-219 and its potential impact for the diabetes treatment landscape and for patients.

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 clinical and preclinical 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 developments 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 undue reliance on the forward-looking statements made today.

I will now turn the call over to Professor Rohit Kulkarni. Rohit?

Rohit Kulkarni: Thank you, Ramses. I started off my career as a physician working in a diabetes clinic in England in Hammersmith Hospital. Simultaneously, I decided to work on a PhD program at the University of London, also at Hammersmith Hospital to gain a deeper understanding of the research work being conducted in diabetes.

So, over the years, I have used both of these experiences as a physician and a scientist to help address the problems we are facing with type 2 diabetes in general. As Ramses mentioned, I'm currently a physician scientist at the Joslin Diabetes Center in Boston. And as the name implies, Joslin does everything that relates to diabetes. So, typically, a given institute does multiple things under a larger umbrella, but here at the Joslin, we are solely working on multiple aspects of one disease and that's diabetes.

Let me start off with a profound congratulations to the team Biomea for reaching this very important milestone in obtaining its IND accepted by the FDA, and now beginning to expand its ongoing clinical trial to those patients with type 2 diabetes in the United States. There are many trials ongoing in diabetes. If you open up clinicaltrials.gov, you will be overwhelmed by the sheer plethora of all of them, each one of them striving to improve the health and wellbeing of diabetes patients.

However, there is no other trial I'm aware of that is aiming to address diabetes as the root cause as Biomea is by reestablishing the pool of functional beta cells the patients once had, and with an oral agent. So, I'm really excited to watch this trial and to see this molecule progresses to the clinic in the months to come.

What Biomea has accomplished so far in preclinical models presented this past summer at the American Diabetes Association's annual meeting and is now pursuing in humans in a Phase 1/2 clinical study is highly relevant and highly novel and significant for patients with diabetes. We have not seen an oral agent such as the BMF-219 that can disrupt the key protein called menin which restricts the proliferation of cells including beta cells. And as we know, these beta cells are key to proper glucose control.

Let's take a look at the background of this disease. Type 2 diabetes occurs when the amount of hormone insulin in the body is unable to maintain normal glucose levels. And this can occur because of a multitude of factors. Chief among these factors is the inability of the body's beta cells to produce appropriate amounts of functional insulin. These cells are either depleted or overburdened, leaving the remaining pool of beta cells unable to produce the functional insulin required.

Beta cells reside in the pancreas and their main function is to produce, store, and release insulin. They're responsible for ensuring glucose levels in blood are within the range that is necessary for an individual to carry out their daily routine activities and ensure that the glucose will not go too high or fall too low. If your beta cell mass is low and your body, therefore, is not producing sufficient amounts of insulin to absorb glucose, sugar levels will spike and this condition over the years will then impact various vital organs causing serious health problems and reducing life expectancy.

In fact, 80% or more of those with diabetes will die from it. Diabetes is a slow killer. An individual with diabetes who does not have sufficient amounts of insulin and, therefore, needs to exogenously inject insulin. While patients have clear and obvious glycemic control benefits from this kind of injected insulin approach, there are many risks and morbidities associated with chronic insulin injections.

The amount of insulin required and injected, unfortunately, is not precise for each individual. And the control of glucose levels, therefore, is frequently less than optimal. This leads to a series of processes in the body which, unfortunately, can end up with serious health consequences and damage to vital metabolic organs. Specifically, these complications can affect the kidney, affect the eyes, affect the cardiovascular system as well as the nerves.

Therapies that can reestablish the pool of beta cells to beta cell proliferation and beta cell reactivation to produce desired amounts of insulin, I'm afraid, do not exist at the moment. Most of the therapies and recommendations that we have available today have only indirect effects on the beta cells, and their effects are temporary. Over time, they have a tendency to fail and most patients end up requiring insulin injections.

There are no therapies that can directly affect beta cell function or regenerate endogenous beta cells, thereby addressing this health condition on the root cause level, which of course would be highly desirable. In addition, it would be remarkable to be able to provide such a disease modifying medication with a short-term treatment duration as an order form for patients.

As we know from experience, the injectable administration of many diabetes medications is a key reason why individuals decline treatment or don't adequately comply with the treatment regimen. This failure to consistently adjust their insulin levels translates to poor disease control and poor outcomes.

Let's now turn to the role of menin in diabetes. When studying the regular function of the pancreas, you will detect proteins which are involved in the growth of beta cells but you will also find some that are responsible for halting or breaking their growth, preventing these beta cells from growing. We, of course, hear a lot about immune checkpoints and their role in blocking the body's immune response to cancer, but we don't often hear about the checkpoints that play a role in diabetes.

Chief among these is a scaffold protein called menin. Menin is one of the endogenous proteins which is critical to regulating beta cell proliferation. And medication that could limit the effect of menin and thereby release the brake that limits beta cell growth, would theoretically allow the beta cells to once again begin to proliferate.

The increase in beta cell mass could then in turn provide diabetic patients with improved glycemic control and would resolve the diabetes symptoms. The repopulated functional beta cells would be capable of producing the right amount of insulin and their normal function restored. This would be a disease-modifying treatment versus one that addresses solely the symptoms of diabetes like all of the available treatments today.

What's particularly exciting is that this approach of enabling beta cells to proliferate and grow again should have positive implications not only for type 2 but also for type 1 diabetes. Over the last 30 years or so, we have mainly targeted the immune system with our type 1 diabetes research and have largely not moved forward because of limited patient benefits.

The current thinking based on a number of studies are used for supporting the proliferation and reactivating of existing beta cells simultaneously with immune suppression. Therefore, any molecule which could enhance growth or proliferation of functional beta cells in a measured way should provide benefits to both type 1 and type 2 diabetes patients. And for that matter, also for pre-diabetes patients who have started down the path of losing their functional beta cell mass.

The data that Biomea shared this summer at the American Diabetes Association meeting and later in the fall at the European Association for the Study of Diabetes meeting further demonstrated the relevance of menin inhibition with an oral agent like the BMF-219. The

data clearly shows that BMF-219 led to the control of key diabetic markers in two standard but different diabetes animal models.

In these experiments, the treatment seemed to control glucose very effectively by promoting the increase of insulin levels and normalizing glucose levels. The results produced by covalent inhibition of menin inferred that this molecule BMF-219 potentially has effects that's directly impacting the proliferation of functional beta cells.

Covalent menin inhibition with BMF-219 also showed that even after the drug was stopped, during the washout period, the effect on blood glucose control continued, providing us an intriguing possibility that this medication could potentially have longer term benefits for diabetes patients after only a short treatment duration. These data showed us for the first time, excitingly, that if you can just stop menin inhibition with an oral agent, you can recover the pool of functional beta cells with effective beta cell proliferation.

As a scientist working in the beta cell field for the last two decades, I'm very excited. An oral agent that directly disrupts menin and, therefore, creates the possibility to regrow beta cells would potentially impact a large number of diseased diabetes individuals.

I'm really looking forward to lead outs from the ongoing Biomea trial of BMF-219 in type 2 diabetes patients. Thank you. I will turn the call now over to Dr. Morris, the Chief Medical Officer of Biomea.

Dr. Steve Morris: Thank you, Dr. Kulkarni, for that very helpful introduction. And hello to the listeners on this call. There are very few novel modalities that are being advanced for the treatment of diabetes. In the context of type 2 diabetes, the chronic use of various agents available today is only effective at reinvigorating the remaining pool of beta cells for diabetic patients. In fact, many of the currently available therapies are just putting more stress on the limited remaining pool of beta cells.

Treatments that address the underlying cause of diabetes, which is the depletion and loss of healthy functional beta cells, remain a significant unmet need and a challenge to develop. The preclinical data our team at Biomea has generated so far with our covalent menin inhibitor BMF-219 in oncology has been quite remarkable. However, the data we have now generated in the standard diabetic preclinical models I find historic.

There is no other agent that has been able to produce data as we have in the recovery of beta cell levels and normalization of insulin production in these animals. With the acceptance of our U.S. IND as announced yesterday, we now have the opportunity to reproduce these results in type 2 diabetic patients and hopefully shift the available treatment paradigm for them.

I would like to direct your attention to the first slide presented as part of this call which describes the typical decline of beta cell mass and function and the concurrent decline of insulin output. This is the reason patients require insulin injection at some point after

other therapies have failed. We are addressing this patient population with BMF-219 in our Phase 1/2 study, COVALENT-111.

Put simply, these patients do not have enough functional beta cells. The regeneration of beta cells could provide a significant improvement in their diabetes disease control and avoidance of diabetes-associated complications such as damage to the heart and blood vessels, the kidneys, eyes, nerves, feet, and other organs.

Now, some details on the COVALENT-111 study design. COVALENT-111 is a randomized, double-blinded, placebo-controlled study. The Phase 1 portion of the study, which has now been completed, consisted of four single ascending dose cohorts assessing BMF-219's effect in healthy volunteers under fasting conditions.

In the Phase 2 portion of the study, the multiple ascending dose cohorts will enroll approximately 100 type 2 diabetes patients who are being concurrently treated with standard of care which includes lifestyle management and/or one or several oral anti-diabetic medications, such as metformin, SGL2 inhibitors and GLP-1R agonists. Just like in the real world, these patients are considered uncontrolled and will stay on their current therapy which is not controlling their diabetes progression sufficiently.

In the Phase 2 multiple ascending dose cohorts, we are testing a total of four different dosing levels, randomized five to one, to receive either BMF-219 or placebo. The goal of the study is to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of BMF-219 in healthy subjects and in subjects with type 2 diabetes at various dose levels.

We are administering BMF-219 once daily for four weeks to explore the potential improvement that it can provide to diabetes patients in maintaining glycemic control. The Phase 2 portion is now enrolling fairly typical type 2 diabetes patients with beta cell deficiency and whose diabetes is not sufficiently controlled with their current therapies. These are adult patients aged 18 to 65 years old, diagnosed with type 2 diabetes within the last 15 years and with their hemoglobin A1c outside of the normal range at screening.

We started enrolling in several centers in Canada earlier this year and are now initiating centers in the U.S. with the same protocol between these two countries. We already completed Phase 1 and available safety and PK data was reviewed by the study safety committee prior to our initiation of Phase 2.

BMF-219 was generally well-tolerated and did not raise any safety or toxicity concerns. We plan to report the Phase 1 details at a scientific conference in 2023.

With COVALENT-111, we eagerly look forward to seeing how the early preclinical results we've seen with BMF-219 translates to humans. Like all Phase 1/2 studies, we will define the proper dose. We will also determine the impact of the duration of dosing and assess the durability of the effect that brings patients back to their normal hemoglobin A1c levels.

We will be using all of the standard type 2 diabetes criteria such as glycemic response to oral glucose tolerance testing, continuous glucose monitoring, hemoglobin A1c, C-peptide, insulin and other exploratory biomarkers. As the diabetes population is very heterogeneous, our biomarker design will allow us to explore high responder subsets.

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

Tom Butler: Thank you, Steve. Today, diabetics have many therapeutic options to treat the symptoms of their disease and regain glycemic control. Unfortunately, none of the available therapies treats the root cause of the disease, beta cell loss.

Over time, these treatments lose their ability to maintain glycemic control, and explains why approximately 10 million diabetes in the U.S. are on insulin. So, how exactly does BMF-219 work and what led to these historic preclinical results on beta cell proliferation?

As Steve explained, the BMF-219 takes the brakes off a key checkpoint that is established in our bodies to prevent beta cell proliferation, the protein menin. As we form a covalent bond to inhibit menin in the pancreas, the body should be able to restore its own beta cell balance. Those cells, as you've heard throughout today's presentation, are necessary to produce sufficient insulin.

We believe by directly and covalently binding to menin, BMF-219 is triggering three key mechanisms that impact the health of an individual's beta cells. One already described, the proliferation of beta cells; two, the reactivation of inactive beta cells; and three, the preservation of existing beta cells.

These effects should not only provide benefits to type 2 diabetic patients, but also those with type 1, as well as obese and pre-diabetic individuals. It is important to recognize that we believe there are three benefits to BMF-219 treatment -- beta cell proliferation, beta cell reactivation, and beta cell preservation.

Therefore, BMF-219 has the potential for broad utility across both type 2 and type 1 diabetes. We saw this measured effect in the Phase 1 portion of covalent 111. That is, in healthy subjects who had normal glucose levels, BMF-219 showed no impact.

What we are leveraging here is nature's biology. We plan to dose patients only for a short, limited amount of time, basically as needed to sufficiently rebalance their beta cells. And from there, their bodies take over. Many may not know but nature provided us with a clue, and it is menin, that controls beta cell growth. And this is actually why we are targeting menin today for diabetic patients.

Beta cell regeneration was detected in pregnant mice by researchers in 2007, just down the road from Biomea headquarters at Stanford. It was observed that pregnancy stimulates the proliferation of maternal pancreatic islet beta cells.

The researchers detected that the hormone prolactin directly inactivates MEN1, the gene responsible for the production of menin. Prolactin represses pancreatic islet menin levels, which in turn stimulates beta cell proliferation.

This physiologic inhibition of menin function in pregnant women allows the larger pool of beta cells to increase insulin production by 200% to 300% and thereby process elevated sugar levels that are associated with the growth of the fetus.

Stanford researchers found that this inhibition of menin is what prevents gestational diabetes. These results built the early understanding of the mechanisms underlying diabetes pathogenesis and revealed that the inhibition of menin could provide a potential target for therapy in diabetes.

With that knowledge, we started our work more than five years ago. The understanding of the function of menin and a deep understanding of the protein's molecular structure served us well as we designed BMF-219 to effectively address menin.

We decided to create BMF-219 as an oral covalent binder to menin. Covalency provides us with an optimized modality of inhibition and affords a greater therapeutic window with higher selectivity and deeper target inactivation.

We believe the covalent binding modality of BMF-219 is the key reason we are passing the higher safety standards required for dosing diabetic patients. From our preclinical work, we know that BMF-219 is inhibiting menin very effectively, and thereby expanding and normalizing the beta cell mass and improving the health and effectiveness of beta cells.

COVALENT-111 will help us now understand the degree of the improvement and the duration of improvement in humans. Based on the preclinical work we completed, we believe we may only need a short-term induction therapy, which we will follow with maintenance on an as needed basis.

Our preclinical models also indicate that the effective dose of BMF-219 in diabetes patients will likely be lower than the dose for oncology patients. We therefore believe we can achieve a meaningful first clinical data set from the Phase 2 portion of COVALENT-111 as soon as the first half of next year.

Thereafter, we plan to continue to release patient data as we achieve longer observation periods. In our animal study, presented at ADA this past summer, we were able to show more than a 3% absolute decrease of hemoglobin A1c with the use of BMF-219.

Several KOLs mentioned to us that a 1% decrease in hemoglobin A1c would be an incredible achievement for an oral agent like BMF-219. As Dr. Kulkarni described, we will be the only therapy in clinical trials to address the long-term health and effectiveness

of beta cells directly with an oral covalent small molecule, focusing on the root cause of type 2 diabetes-the depleted pool of beta cells.

In closing, I want to thank the Biomea team for achieving this incredible milestone ahead of schedule. My teammates here are incredible professionals and they are executing at a very high level. We are now looking forward to getting the clinical sites here in the U.S. initiated and the first U.S.-based patients enrolled. Let's open the floor now for questions.

Operator?

QUESTIONS AND ANSWERS

Operator: Thank you. (Operator Instructions). Our first question comes from the line of Joseph Catanzaro from Piper Sandler. Your line is now open.

Joseph Catanzaro: Hey, guys, thanks for hosting us. And thanks for taking my questions. Maybe just a few for me. So over the weekend at ASH, I think we saw some discussion around the tissue distribution of a menin inhibitor and how that potentially impacts the clinical profile. So wondering if you could speak to 219's tissue distribution profile and how that could play a role within the context of diabetes and maybe also touch on the oncology indications that you're pursuing.

And then, as a follow up, it sounds like patients are likely to be on a number of potential background therapies. So are there any drug-drug interaction concerns that you're aware of or we'll be monitoring that might impact the exposure of 219 or exposure of even the background therapies? Thanks.

Tom Butler: Yes. Thanks Joe. I can take the tissue exposure question, and the initial DDI question, I will hand it over to Steve for follow up. 219 does an incredible job of penetrating key tissue compartments like the pancreas. And I think that's what first gave us initial clue that oncologically, we could get the concentrations you need in the pancreas that would generate an effective response.

And so that gave us initial clue on how to calculate the dose groups that you see from the ADA and ESAD poster presentations. And thinking about the translation to oncology that also really encourages us for obviously the COVALENT-102 solid tumor trial that's enrolling lung, pancreatic cancer and colorectal, knowing that 219 does really a great job of getting tissue penetration. And we think that the dose level as mentioned in the call, the dose level for type 2 diabetes should be much lower than what we expect to move forward with in oncology. Steve?

Dr. Steve Morris: Certainly happy to speak to the question regarding DDI. The short answer is there are no obvious liabilities in that respect. We are allowing a broad spectrum of standard of care type 2 diabetes agents for patients who are enrolled in 111. So, again, we do not anticipate any substantive DDI issues with chronic use type 2 diabetic agents.

Tom Butler: Thanks, Steve. Yes, so patients can take Metformin, they can be on a GLP-1. They can be on an SGLT2, for example.

Joseph Catanzaro: Okay, great. That's helpful. Maybe just one quick follow up as it relates to A1c. Tom, I know you mentioned, sort of, 3% reduction in the preclinical models, and then 1% reduction as the hurdle sort of set by KOLs. I'm wondering if that, sort of, within a 28-day period, if you would expect to see some of those changes to that degree? Or is that something that might take just a little bit longer follow up to materialize?

Tom Butler: Yes. When you're on drug for four weeks, certainly hemoglobin A1c reduction won't be optimized because hemoglobin A1c is really a 90-day look. But you will be able to see the initial reduction. What you should be looking for is what's the reduction in blood glucose, because over time when hemoglobin A1c will show as we get further duration data from the patients. But certainly C-peptide insulin production, beta cell efficiency and blood glucose are kind of those four-week look data cuts.

And then you want to see an initial decline or see initial slope in the hemoglobin A1c and you want it to continue obviously as drug is pulled, but the key for us is, we don't know if it's four weeks. We don't know if it's six or eight, based on our mathematical modeling and somewhere in that range. And now we just have to assess in this multiple ascending dose cohort design, what's the right dose level and what's the right time frame.

Joseph Catanzaro: Okay, perfect. Thanks so much for taking my questions.

Tom Butler: Absolutely.

Operator: Thank you. One moment for our next question. Our next question comes from the line of Eric Joseph from J.P. Morgan.

Eric Joseph: Hi, guys. Good evening, and thanks for taking the questions. Just a couple from us. First, Tom, you highlighted the example, I guess the pattern of menin-mediated glucose control in pregnant women. Is it clear that menin expression is dysregulated in diabetic or pre-diabetic patients? Like if it's regulated and that, I mean, overexpression? Is it possible that sort of the menin expression pattern might predict for who might benefit from a menin inhibitor? And I have a follow up to this.

Tom Butler: Yes. I think that's a very good question, sorry you broke up just a little bit in the beginning of the question. But I think I understood it correctly. I think it is a great question, is there a way to check menin expression levels to see who would benefit the most?

That's certainly something exploratory that we could do. But I'm not sure the capability of assessing it in the beta islet versus trying to find a peripheral diagnostic to assess. But I think for us diabetes has several subtypes, right? And that it's well-known what they

suffer from, whether it's severe insulin resistance, or a depleted pool. And really, if you track the C-peptide and insulin production over time, you get a sense of how that pool is continuing to deplete. And so for us the key is to try to capture these patients who have somewhere between 40% to 60% of their pool and see how much increase we can elicit with BMF-219. And what impact on glycemic control we can elicit, if that makes sense.

Eric Joseph: Yes, yes. And maybe just to expand on that last point in terms of how you're tracking. What biomarkers in particular are you tracking as a measure of beta cell proliferation as part of the Phase 2 portion? Do you need to track patients for some period to sort of establish a baseline measure? When you say sort of in a certain pool, I guess, how long does it take to establish that baseline? Thanks.

Tom Butler: Yes, exactly. It's a really good point. And obviously, when we enroll these patients, we'll understand their current C-peptide, which is a stable measurement of their insulin production and their insulin production directly. And what we'll do is we'll track how BMF-219 increases that production or the efficiency of their beta cells, how much insulin production is required to achieve glycemic control and get an understanding of what does that look like at the four-week cut. And then, as we monitor patients long-term, we hope to see that that production is maintained.

Eric Joseph: Great, thanks for taking the questions for us in the session.

Tom Butler: Absolutely.

Operator: Thank you. One moment for our next question. Our next question comes from the line of Michael King from EF Hutton.

Michael King: Good afternoon, guys. Thanks for doing this call. It's been really helpful. Tom, I just wanted to ask you to maybe drill down a little bit deeper on the comment you made a few moments ago about the amount of pancreatic reserve. Did you say 40% to 60% is what you're targeting?

Tom Butler: Yes, initially, I mean, it could even go down to 35%. But it's in that range of 40% to 60%. of remaining pool based on time of first diagnosis.

Michael King: And then are you going be looking at fructosamine, as well as for a short-term measure of A1c?

Dr. Steve Morris: This is Steve Morris. Yes, indeed, we will be looking at fructosamine. For those of you who are not aware, fructosamine provides as a clue, a snapshot as it were, into longer term glucose control, similar to A1c but unlike A1c, fructosamine provides an earlier peek as to the extent of that longer term glucose control. Yes, indeed, we will be assessing frustosamine in our patients.

Michael King: Okay, thanks for that. And then just finally, I wonder if you could talk sort of more holistically, obviously, beta cell proliferation, preservation and glucose control is

critical. But I just wonder from the standpoint of the therapeutic milieu with GLP-1 and SGLT2, etc., you're getting sort of more holistic approaches to the management of type 2 diabetes with weight loss and cardiovascular benefit, etc. I just wonder, can we speculate a little bit about how menin might play into the features and benefits of other competing oral agents? Thanks.

Thomas Butler: Yes, it's a really good question, Mike. And I think this took us to have a deeper understanding of the disease and learn that, look, the current treatment paradigm is focused on reducing blood sugar, but it's reducing blood sugar by either exerting more workload, more exhaustion on the existing pool, or increasing filtration rates of blood glucose.

If you look at it from that perspective, no one is really directly addressing the disease, which is a depleted pool of beta cells. And so, for us to come in as an oral therapy as an oral agent, and the convenience of such where we're not actually inhibiting or implicating those other mechanisms of action, if anything, we would be making them better, first of all. And then the broad utility, given the novel MOA of BMF-219, just allows us to focus on this beta cell health as the paradigm shifts. And I think, if we can set that as the first step, this will really be a paradigm shift for not only the injectables, but you see that a lot of these other agents are trying to shift to oral therapy, because you have lack of persistence, lack of compliance. And then as I mentioned in the conference call script earlier, there's a reason why there's 10 million type 2 diabetics on insulin, because the current existing landscape has failed them. And they will, over time, no question. And so, we want to prevent that from happening and really focus on the root cause of the disease.

Michael King: Okay, sorry, if I could just sneak in one more quick question here. And that is, any intention to study type 1 diabetes? And if so, again, what kind of, I imagine they have to have at least some residual pancreatic reserve before you could put them in study, but what's the current plan if any?

Thomas Butler: Yes, absolutely. So with type 1, certainly our interest is quite high in this area. And as we produce proof-of-concept data, and the strength of that data, that will encourage us to go into type 1 diabetes. Certainly these folks at clinical diagnosis, they have 10% or less of a remaining pool. And so, we want to first obviously explore in patients that have more of an existing pool, and then take it to the next step. And just to add, sorry, just add little bit more, I think I didn't address the cardiovascular and the weight loss and those benefits. And I think if you look at those outcome trials and those ancillary benefits, that's really because they're trying to have a way that they look at alternative benefits by not addressing the root cause of disease, if that makes sense. So if you address the root cause of the disease, all those cardiovascular, the weight loss, all those benefits will come over time, because you're achieving the glucose control.

Michael King: Right, right. All right, thanks for taking the questions.

Thomas Butler: Sure.

Operator: Thank you. One moment for our next question. Our next question comes from the line of Hartaj Singh from OPCO.

Hartaj Singh: Hello, everyone, this is Eka dialing in for Hartaj today. Congrats on the IND clearance, and thanks for that update. We have a couple of questions. Firstly, can you talk about what the regulators are looking for in regards to the safety database for diabetes? How long of a follow up will you need in the multiple ascending dose Phase 2? Secondly, what are your thoughts on how long has the dosing duration might be now based on the translational work and preclinical data for BMF-219? And lastly, can you just comment on any strategic plans to conduct type 2 diabetes studies in other countries globally, to potentially expand to other markets? Thank you for taking our questions.

Thomas Butler: Sure, absolutely. Thank you for the questions. And sorry, I missed the initial part about the required follow up from regulators. I didn't catch that.

Hartaj Singh: Yes, sorry about that. So for the multiple ascending dose Phase 2, what are regulators looking for in regards to safety database? How long of a follow up?

Thomas Butler: Yes, Steve, do you want to take that?

Dr. Steve Morris: My pleasure. What I can tell you is that in the COVALENT-111 study, we will be following patients for a total of 26 weeks, of course, to assess durability of glycemic control, but in addition to assess safety and tolerability of 219. And given the fact that the protocol submitted with the IND package received the approval from the FDA, we assumed that that 26 week follow up period will suffice at least at this stage of development.

Hartaj Singh: Thank you. Thank you for the caller.

Operator: Thank you one moment for next question. Our next question comes from the line of Eun Yang from Jefferies.

Eun Yang: Thank you for taking the questions. So a few questions. First, just to clarify the data that we're going to be seeing in the first half of next year, would it be Phase 1, as well as the Phase 2 from all the patients, about 100 patients?

Thomas Butler: Yes, that's a great question, Eun. So the data that we'll provide in the first half of next year will be a combination, it will have some of the Phase 1 PK data, as well as Phase 2 data in the first two cohorts-the multiple ascending dose cohorts at 100 milligram and 200 milligram, who have been dosed for four weeks.

Eun Yang: Okay, thanks. And then 219 works by augmenting beta cell production and function. So I'm kind of wondering why not aiming for normalization of A1c levels instead of a 1% reduction?

Thomas Butler: Yes, so we're not necessarily aiming for a 1% reduction, I think. We were just getting feedback that a 1% reduction with an oral agent is a great outcome. We're obviously internally expecting much more from BMF-219, if that's helpful.

Eun Yang: Okay. And the last question, it might be very naive, kind of dumb question. But is there, aside from looking at A1c, as well as glucose levels, is there another way that you can actually demonstrate that 219 really increases beta cell production and function?

Thomas Butler: Yes, I mean, there is. So what we've been doing within our research team is actually doing ex-vivo work with human micro tissue islets. And there, you can look at beta cell proliferation, beta cell function improvements in the absence and in the presence of BMF-219, versus other mechanisms of action, and assess from that perspective. I think from a clinical trial experiment, it's very hard to assess that you've expanded their pool, other than seeing that the drug has elicited an increase in C-peptide insulin production that resulted in glycemic control or an improvement in glycemic control. And that led to a durable impact, meaning you don't need continuous exposure of BMF-219 to see the benefit. Beta cells have a very long half-life on the order of 10 plus years. So if the efficacy we see has a long durable effect, then we have high confidence that this is due to increased mass invasion.

Eun Yang: I see. I guess kind of a biopsy in the pancreas that probably is not going be approved by the FDA for diabetes?

Thomas Butler: Sorry?

Eun Yang: I mean, a kind of a pancreatic biopsy may not be an option in diabetic trials?

Thomas Butler: No, I don't think so.

Eun Yang: Okay. All right. Thank you very much.

Thomas Butler: Thank you.

Operator: Thank you one moment for our next question. Our next question comes from the line of Justin Zelin from BTIG.

Justin Zelin: Hey, guys, congrats on the milestone. Just two questions for me. The first was from your preclinical data. Have you seen any evidence of weight loss in mice, or do you expect any with this mechanism?

Thomas Butler: Yes, we did. In our publications, we did see weight loss. And I think it's really important to know that look, at the end of the day, if you were able to drive down blood sugar levels, that will lead to benefits and in weight, benefits in cardiovascular outcomes, etc. And really if you're reestablishing the pool of beta cells that the patient

once had, there's going to be, we expect to have many benefits that we'll be able to show from a quality of life perspective.

Justin Zelin: Excellent. And then my only other question was, you're taking an approach here where you're looking towards induction therapy, kind of driving a vast amount of the efficacy here on the population. I was just wondering if you had any durability data from your preclinical work that you'd expect to translate here to give you confidence that you might have a lasting durable effect from the induction therapy perspective?

Thomas Butler: Yes, absolutely. Yes. So in our in our animal model work, we did show durability there, following drug washout. And then the durability really stems from the half-life of beta cells, which is on the order of 10 plus years. So our theory, our primary thesis is that if we're able to reestablish the pool, the pool will have long shelf life, and then allow us to monitor the patients over time and use maintenance therapy as needed. So for us, we don't have to knock it out of the park in the first four to six weeks. Not at all. You just want to see a nice improvement in the first four to six weeks, and then following maintenance therapy or certain intervals we want to be able to maintain over time.

Justin Zelin: Great, that makes sense to me. Well, thanks so much for taking the questions and congrats again.

Thomas Butler: Thanks, Justin.

Operator: Thank you. One moment for our next question. Our next question comes from the line of Matthew Phipps, from William Blair.

Matthew Phipps: Thanks for taking my questions, congrats on the IND clearance. There's preclinical data kind of showing the direct crosstalk maybe between GLP-1 signaling and menin signaling and they might be kind of directly regulating each other. Have you ever pre-clinically, it's kind of the combination of a GLP-1 agonist and your menin inhibitor, and do you think that can be teased out in the clinical trials?

Thomas Butler: Yes, so certainly in COVALENT-111 patients will be enrolled while on a GLP-1. So there will be that efficacy data, if there is an additional benefit of adding on 219. And I think it's really important for everyone to know that, look, at the end of the day, COVALENT-111 is enrolling patients who are on standard of care. And it can be on mono, they can be on two therapies or are on three therapies at most. And the hemoglobin A1c is rising, and it's at anywhere between 7% and 10%. So they're well uncontrolled. And so, if we can introduce BMF-219 to restore glycemic control, it'll be a very exciting result. And I think this is the key patient population to assess. So we'll be able to get a good look on what BMF-219 can do and in combo with metformin, with a GLP-1, with SGLT2, for example. Preclinically we haven't done those combo studies yet.

Matthew Phipps: Yes, thanks.

Operator: Thank you. I would now like to turn the conference back to Thomas Butler, CEO for closing remarks.

Thomas Butler: Yes, thank you guys, everyone for attending this call. These are very exciting times. Look forward to the clinical expansion of COVALENT-111 in 2023, and I look forward to updating you shortly. Take care.

Operator: This concludes today's conference call. Thanks for participating. You may now disconnect.