

Menin Mondays

About Our Clinical Investigation of BMF-219 in Type 2 Diabetes Patients

1. How come you started to develop BMF 219 for diabetes?

With our investigational agent BMF-219 we are addressing the scaffold protein menin, which is thought to be the culprit in the development of diabetes. Diabetes has as its root cause the depletion of beta cells, cells in the pancreas responsible for making insulin. Insulin allows for proper regulation of sugar in your blood to be used for energy. Once the pool of beta cells is depleted it does not easily grow in the presence of menin. In 2007 Scientists at the University of Stanford were able to prove in animal models that menin is directly responsible for preventing the growth of beta cells in the pancreas (Karnik et al. *Science*, 2007). Later in 2010 researchers at University of Pennsylvania validated in animals that the inhibition of menin leads to improved glycemic control, correcting diabetes (Yang et al., 2010). The Biomea research team applied these findings for the first time ever in diabetic patients, using its covalent menin inhibitor BMF-219 in a human clinical trial -- COVALENT 111. BMF-219 is studied here for its potential impact on normalizing glucose levels in diabetes.

2. Is there even a need for another agent in the field of diabetes?

"Diabetes is a common disease that affects nearly 40 million people in the U.S. and is projected to affect more in the coming years. The need for more antidiabetic treatment options is clear," says Lisa Yanoff, M.D., deputy director of the Office of Cardiology, Hematology, Endocrinology, and Nephrology in the FDA's Center for Drug Evaluation and Research on May 25, 2023.

The currently approved therapies are all for chronic use, they typically work only for a limited period of time only, produce unwanted side effects and are in the main ameliorating symptoms. They are not addressing the root cause, beta cell depletion, which continues during the progression of Type 2 Diabetes. As Dr. Yanoff from the FDA indicates, "the need for more antidiabetic treatment options is clear".

Menin Mondays

About Our Clinical Investigation of BMF-219 in Type 2 Diabetes Patients

3. How is the study of BMF-219 in diabetic patients structured?

Our clinical trial studying BMF-219 in Type 2 Diabetes patients (COVALENT 111) is the first of its kind. This is the first clinical trial study ever to pursue long-term glycemic control for patients with Type 2 Diabetes by addressing the root cause of the disease. This is also the first time an agent has entered clinical trials with the aim for long term benefit after a short treatment period for patients with Type 2 Diabetes. We are currently in dose escalation phase, here we are testing BMF-219 at various dose levels to assess the safety, tolerability, and the level of glycemic control while on treatment. In this phase, we are only dosing for 4 weeks. Once we have completed the dose escalation phase, we will expand two of the dose levels. In the expansion phase, we plan to dose for longer periods of time, up to 12-weeks. This will allow us to understand the optimal period of treatment for patients with different background characteristics. We want to ensure we have optimized the dose level as well as the dosing duration to ensure we effectively support the largest number of diabetic patients with the longest duration of effect.

4. Is the investigative use of BMF-219 any different than the standard of care diabetic agents?

In our study COVALENT 111, we are testing various dosing intervals to reestablish the pool of beta cells in diabetes patients. These cells will help normalize the insulin production and sensitivity as nature intended it. We think these effects will provide continued glycemic control even after a short dosing period. There is no agent approved in the US today that is only used for an initial dosing period providing lasting effects thereafter. All agents in use are chronic therapies and none have pursued BMF-219's mechanism of action, the covalent inhibition of menin. Commercially used agents are primarily addressing the symptoms of the depleting pool of beta cells, rather than the root cause of diabetes.

Menin Mondays

About Our Clinical Investigation of BMF-219 in Type 2 Diabetes Patients

5. What is a typical therapeutic approach to treat a patient with Type 2 Diabetes and how does it compare to BMF-219?

BMF-219 is an oral agent that is currently investigated for various dose levels and dosing durations in a clinical trial (COVALENT 111). BMF-219 is addressing diabetes quite differently from all other therapies currently used commercially. BMF-219 is covalently inhibiting a key protein -menin- to allow for the regeneration, preservation, and reactivation of beta cells, which are the insulin producing cells in the pancreas. After an initial dosing period, we expect BMF-219 to be used only when and as required to maintain the achieved rebalancing of the pool of beta cells.

There are over 60 approved single and combination agents in the market today. All agents are chronically prescribed. As an agent is failing to continue to provide benefits, physicians are adding other agents to the regimen or change the original agents used to regain glyce-mic control for patients. Patients cycle through each agent and use them as long as they provide benefits. Of all patients treated in the US, about 50% of patients still fail to achieve their A1c goal of <7% (as published in N Engl J Med 2021;384:2219-28. DOI: 10.1056/NEJM-sa2032271). Typically patients start their journey with an oral anti-diabetic drug, like Met-formin, added or followed by DPP-4 Inhibitors, SGLT2 Inhibitors and oral/ injectable GLP-1 receptor agonists. Once all drugs and drug combinations are no longer supporting the patient then injection of pure insulin is the only available treatment. Today approximately 30% of Type 2 Diabetes patients either use insulin alone or in combination with an oral agent.