

# Menin Mondays

## About BMF-219's Breakthrough Approach to Address Diabetes

### 1. How does BMF-219 work?

BMF-219 targets a transcriptional scaffold protein, menin, which is thought to act as a brake on beta-cell turnover and growth. Beta cells are found in your pancreas and are responsible for producing and regulating the right amount of insulin in your body to control blood glucose levels. By inhibiting menin, we are investigating whether BMF-219 has the potential to safely increase the pool of healthy insulin producing beta cells for people living with diabetes. There are three mechanisms which may improve glycemic control: 1) proliferation of beta cells (2) preservation of the existing beta cell pool (3) reactivation of dormant beta cells.

### 2. How could BMF-219 be different than other type 1 and 2 diabetes treatments?

Unlike currently approved diabetes treatments, BMF-219 is being studied in clinical trials to determine its potential to safely provide long-term glycemic control by restoring the patient's pool of healthy beta cells. We believe there are no currently available medicines designed to address this underlying cause of diabetes - the depleting pool of healthy beta cells.

### 3. I've seen you mention that there is 'biological precedent' for how BMF-219 works. What do you mean?

A biological precedent provides researchers with scientific support and a higher degree of certainty in their approach when addressing new targets. As it relates to menin, during pregnancy, the female body increases a hormone – prolactin – that downregulates menin and thereby has shown to increase the pool of beta cells. This increase in beta cells leads to a higher production of insulin and allows the pregnant mother to address the increased glycemic burden from the growing fetus. This observation has inspired Biomea to further research the function of menin in diabetes.

(Ref: Karnik et al., *Science*. 2007 DOI: 10.1126/science.1146812)

### 4. Patients with diabetes must take their medication for the rest of their lives chronically in order to maintain benefit, in many cases these therapies fail after several years. Would BMF-219 be the same?

Because of BMF-219's potential to proliferate beta cells, preserve the existing beta cell pool and reactivate dormant beta cells, Biomea is examining BMF-219 as a short-term (estimated between 4-12 weeks) treatment, with the potential to be followed by a prolonged period of glycemic control after the treatment has ended. BMF-219 is also an oral agent.

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### 5. Do you know how long it may take for a diabetic patient treated with BMF-219 to see durable improvements in glycemic control?

A response to BMF-219 will depend on the existing depletion of the pool of a patient's beta cells and the health of the remaining beta cells. In addition, each patient will have their own proliferation rate. This question is being examined in the ongoing COVALENT-111 study.

### 6. Once a patient's glycemic control improves, will they need to keep taking BMF-219?

Based on the mechanism of action, we are investigating the potential for BMF-219 to be used as a short-term treatment that can be halted once sufficient glycemic control is achieved. This question is being examined in the ongoing COVALENT-111 study.

### 7. How long could the effect of BMF-219 last?

This depends on what caused the benefit achieved with BMF-219. A benefit could have been caused by any of the various factors observed in pre-clinical studies: proliferation of beta cells, improvement of insulin resistance, reactivation of beta cells, or the preservation of beta cells. Each of these effects may have a different duration of effect. This question is being examined in our ongoing COVALENT-111 study.

### 8. Why is BMF-219 being studied in both diabetes and cancer?

As a scaffold protein, menin can interact with hundreds of different partner-proteins, which help regulate a wide range of cellular functions including transcription, DNA damage repair, cell signaling, cell division, proliferation, and migration (*Ref: Biancaniello et al., Molecules. 2022 DOI: 10.3390/molecules27051747*). Therefore, inhibiting menin can be useful in various disease settings where its function is critical to the disease progression.

### 9. Is taking BMF-219 safe for a diabetic patient?

This question is being examined in our ongoing COVALENT-111 study. BMF-219 was generally well-tolerated in its first clinical data release of its first two dosing cohorts after 4 weeks of dosing. So far, no patient on BMF-219 discontinued dosing and all patients completed 4 weeks of treatment.