QUICK FACTS – BMF-219 in Oncology

Biomea's Investigational Covalent Menin Inhibitor

What is BMF-219?

Our lead product candidate, BMF-219, a synthetic chemical compound (also described as a small molecule), is designed to be a potent, selective, orally bioavailable, covalent inhibitor of the protein menin, a critical regulator known to play a direct role in oncogenic signaling in multiple cancers. A covalent inhibitor is an inhibitor that binds to a target and then forms a permanent bond with it. Covalent binding molecules, like BMF-219, show high potency with low molecular mass (i.e. overall size of the small molecule), providing better availability within the body and a larger therapeutic window than reversible drugs can typically achieve.

What is menin?

Menin is a scaffold protein that impacts multiple cellular processes including cell cycle control, apoptosis, and DNA damage repair through interactions with dozens of different binding partners. It plays an essential role in oncogenic signaling in multiple cancer types.

How is BMF-219 designed to work?

In oncology, BMF-219 is designed for the treatment of cancers that are highly dependent on menin by inhibiting the interactions between menin and its binding partners via a permanent chemical modification. BMF-219 is designed to form a **covalent** bond with menin, and permanently block the interaction between menin and numerous binding partners which could lead to a more pronounced beneficial effect than reversible inhibitors. BMF-219 has shown the ability to modulate the expression of MLLr, NPM1, MYC and KRAS in preclinical models.

What is special about BMF-219?

Covalent drugs have shown the potential to offer advantages in safety, tolerability and efficacy over conventional reversible drugs. Other drugs that try to prevent the interaction between menin and its binding partners work through a **reversible** mechanism. That means the drug undergoes continuous cycles of binding and release from its target. Thus, constant coverage at high continuous systemic exposure in the body is generally needed with a reversible inhibitor, which can pose safety and tolerability challenges. In contrast, BMF-219 is designed to work through an **irreversible** mechanism, a covalent bond. That means BMF-219 is designed to form a permanent bond with menin preventing a protein molecule from ever binding again. In addition, the effect of an irreversible drug is designed to remain even after the body has cleared the drug because the target protein is permanently disabled.

Oncology Programs with BMF-219

BMF-219 is a covalent menin inhibitor being developed for the treatment of cancers that are highly dependent on menin. We are currently developing BMF-219 for the treatment of cancers including MLL-r AML, NPM1 mutant AML, high-risk CLL, MYC driven/addicted liquid tumors (e.g., DLBCL and MM), and KRAS mutant

colorectal, lung, and pancreatic tumors. As of December 31, 2022, BMF-219 is being evaluated in up to 8 liquid and solid tumor types in two ongoing clinical trials.

COVALENT-101: BMF-219 in Menin-Dependent Hematologic Malignancies

COVALENT-101 is a Phase 1 clinical trial to explore the safety and efficacy of BMF-219 in patients with relapsed /refractory acute leukemias (AML and ALL), including those with MLL/KMT2A gene rearrangements or NPM1 mutations. The study includes various cohorts of patients to explore the potential utility of BMF-219 across a range of menin-dependent hematologic malignancies including multiple myeloma (MM), diffuse large B-cell lymphoma (DLBCL), and chronic lymphocytic leukemia (CLL). The first patient was dosed in January 2022 and enrollment is ongoing (NCT05153330).

COVALENT-102: BMF-219 in KRAS Mutant Solid Tumors

COVALENT-102 is a Phase 1/1b dose finding study evaluating the safety, tolerability, and clinical activity of escalating doses of BMF-219 in patients with unresectable, locally advanced, or metastatic non-small cell lung cancer (NSCLC), colorectal cancer (CRC) and pancreatic ductal adenocarcinoma (PDAC) with an activating KRAS mutation. The first patient was dosed in January 2023 and enrollment is ongoing (NCT05631574).