# QUICK FACTS – BMF-219 in oncology

**Biomea's investigational covalent menin inhibitor**

## *What is BMF-219?*

Biomea's investigational oral, small molecule, BMF-219, is designed to be a potent, selective covalent inhibitor of the protein menin. Menin is a critical regulator known to play a direct role in oncogenic signaling in multiple cancers[1]. A covalent inhibitor binds to a target and forms a permanent bond with it. Optimized covalent binding molecules, like BMF-219, can show high potency with lower systemic exposure, allowing for a larger therapeutic window than what many 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[2].

## *How does BMF-219 work?*

In oncology, BMF-219 is being examined for the potential treatment of cancers that are highly dependent on menin. BMF-219 is designed to form a **covalent** bond with menin, and thereby permanently block the interaction between menin and numerous binding partners, which could lead to pronounced beneficial effects. BMF-219 has shown in preclinical models to modulate the expression of target oncogene expression including NPM1, MYC, HOX, MEIS1, BCL2 and KRAS.

## *Why is BMF-219 binding covalently to menin?*

Covalent drugs have shown the potential to offer advantages in safety, tolerability, and efficacy over conventional reversible drugs. Covalent binding can provide three distinct advantages: higher target selectivity, deeper target inactivation and a greater therapeutic window. BMF-219 is a covalently binding small molecule, which has been designed to form a permanent bond directly with menin. This bond is designed to remain in effect even after the body has cleared the drug, as the target protein, menin, has been permanently disabled. Other investigational menin inhibitors in the clinical are typically designed to block the interaction between menin and its binding partner, MLL1, through a reversible mechanism. Reversible inhibitors undergo continuous cycles of binding and subsequent release from their target. Thus, constant coverage at high continuous systemic exposure in the body is generally needed with a reversible inhibitor. This can pose safety and tolerability challenges.

[1] Agarwal SK, et al. *Horm Metab Res* 2005. DOI: 10.1055/s-2005-870139
[2] Matkar S, et al. *Trends Biochem. Sci*. 2013 DOI: 10.1016/j.tibs.2013.05.005

### *Which oncology programs have been started with BMF-219?*

BMF-219 is a covalent menin inhibitor being developed for the treatment of cancers that are highly dependent on menin. Biomea is currently developing BMF-219 for the treatment of cancers including MLL1-r AML, NPM1 mutant AML, high-risk CLL, MYC driven/addicted liquid tumors (e.g., DLBCL, MM), and KRAS mutant colorectal, lung, and pancreatic tumors. BMF-219 is currently being evaluated in up to 8 liquid and solid tumor types in two ongoing clinical trials.

COVALENT-101 is a Phase 1 clinical trial to explore the safety and efficacy of BMF-219 in patients with relapsed/refractory AML and ALL, including those with MLL/KMT2A gene arrangements 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 MM, DLBCL, and CLL (NCT05153330).

We have also initiated and are enrolling COVALENT 102, a Phase 1/1b clinical trial 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 (NCT05631574).