COVALENT FLT3 INHIBITOR BMF-500

Biomea is advancing BMF-500 to clinic with an IND application cleared in 1H2023 and a phase 1 study COVALENT-103 NCT05918692 initiated and first patient dosed in 2H2023.

BMF-500 is an investigational third generation covalent FLT3 inhibitor, which has demonstrated preclinically that it may be the most potent and selective inhibitor of FLT3 evaluated to date:

- **Greater Cytotoxicity:**
  In AML cell lines, three-hour treatment with BMF-500 followed by washout produced higher cell killing than continuous exposure to a non-covalent FLT3 inhibitor

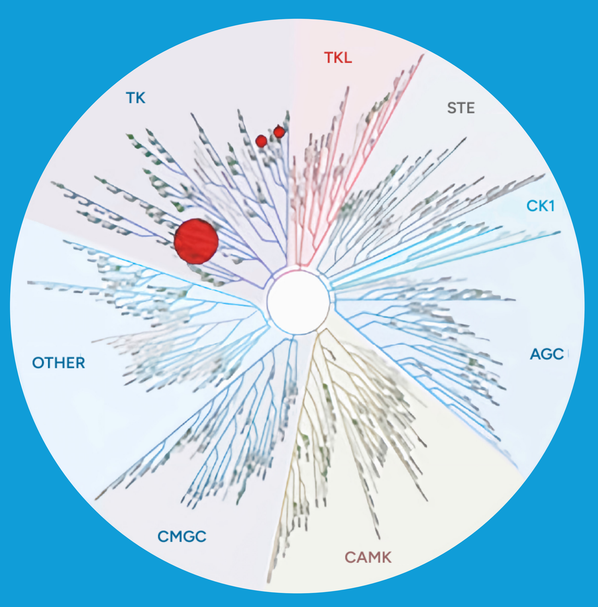
- **Sustained FLT3 Inhibition:**
  BMF-500 elicited complete tumor regression of FLT3-ITD acute leukemia in mouse tumor models and maintained its effect without continued exposure

- **Highly Selective:**
  Kinase panel assay displayed potential best in class selectivity towards FLT3 and picomolar potency

Dose escalation and dose expansion phase 1 trial in progress in U.S.

BMF-500 Kinase Profile

169 Assays Tested
4 interactions mapped



BMF-500 is an investigational, novel, orally bioavailable, highly potent and selective covalent small molecule inhibitor of fms-like tyrosine kinase 3 (FLT3).

BMF-500 was discovered and developed in-house at Biomea using the company's proprietary FUSION™ System and has demonstrated best-of-class potential based on extensive preclinical studies.

The kinase profile of BMF-500 showed high target selectivity, suggesting the potential for minimal off-target liabilities. BMF-500 was designed to have a therapeutic profile to allow for combinations with standard of care and/or novel targeted agents like icovamenib.

FLT3 is a receptor tyrosine kinase (RTK) that plays a central role in the survival, proliferation, and differentiation of immature blood cells. Notably, FLT3 gene mutations are common in patients with AML and are associated with a poor prognosis. Nearly 30% of AML patients have a FLT3 mutation, representing more than 6,000 incident patients in the United States each year. While FLT3-specific and pan-tyrosine kinase inhibitors are approved by the FDA across various lines of therapy in AML, these agents have produced relatively low rates of durable responses, and overall survival remains an unmet need.

Previous data presented at medical conferences showed BMF-500's picomolar affinity to activating FLT3 mutations, including FLT3-ITD and various tyrosine kinase domain (TKD) mutations (Law et al. ASH 2022). BMF-500 demonstrated multi-fold higher potency and increased cytotoxicity than commercially available non-covalent FLT3 inhibitor gilteritinib.

Further data also exhibited the potential utility of combination strategies to achieve higher antileukemic cell killing with reduced concentrations of BMF-500 and icovamenib (Law et al. AACR 2023). These data provide preclinical evidence for combining pathway-specific inhibitors as a promising therapeutic strategy for further investigation in acute leukemia.