QUICK FACTS – Biomea Corporate Overview and Programs

Overview

We are a clinical-stage biopharmaceutical company (NASDAQ: BMEA) focused on the discovery and development of covalent small molecule drugs to treat patients with genetically defined cancers and metabolic diseases. A covalent small molecule drug is a synthetic compound that forms a permanent bond to its target protein and offers a number of potential advantages over conventional non-covalent drugs, including greater target selectivity, lower drug exposure, and the ability to drive a deeper, more durable response. Leveraging our extensive expertise in covalent binding chemistry and development, we built our proprietary FUSION™ System discovery platform to advance a pipeline of novel covalent small molecule product candidates.

Our lead product candidate, BMF-219, is designed to be an oral potent and selective covalent inhibitor of menin, an important transcriptional regulator known to play a direct role in oncogenic signaling in multiple cancers as well as in regulating the growth of beta cells in the pancreas. In preclinical studies, administration of BMF-219 has resulted in robust anti-tumor responses across a range of liquid and solid tumor models and has been generally well-tolerated in animal studies. Additionally, administration of BMF-219 produced a pronounced effect in preclinical models of diabetes as well as in early clinical studies, normalizing glucose levels during treatment and even after cessation of drug treatment. BMF-219 is being evaluated in 8 liquid and solid tumor types and in diabetes across several ongoing clinical trials.

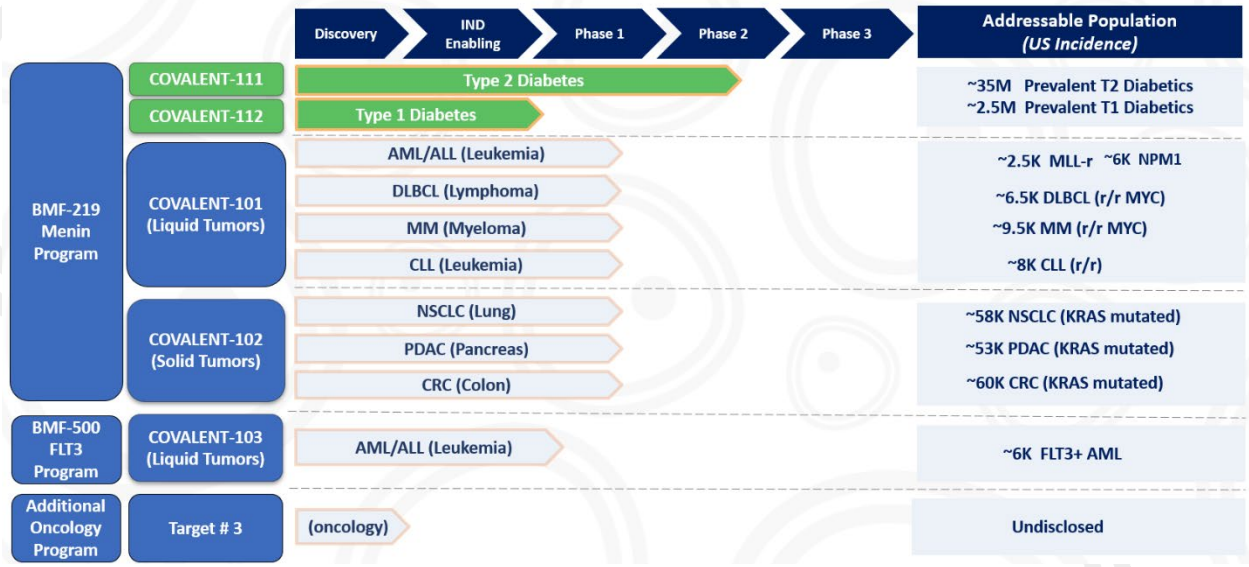
Beyond BMF-219, we are utilizing our novel FUSION™ System to pioneer covalent treatments against other high-value genetic drivers of disease. We entered the clinic with our second development candidate, BMF-500, a covalent inhibitor of FLT3 and are studying BMF-500 in acute leukemia patients. Both molecules, BMF-219 and BMF-500, were developed in-house by the Biomea team.

We are currently advancing additional preclinical covalent small molecule programs for the treatment of select cancers and expect to nominate our third development candidate soon. Our goal is to utilize our capabilities and platform to become a leader in developing covalent small molecules to maximize the depth and durability of clinical benefit when treating various cancers.

After working closely together at Pharmacyclics, our Chief Executive Officer and Chairman of the Board of Directors, Thomas Butler, and Chief Operating Officer and President, Ramses Erdtmann, founded Biomea Fusion in 2017 with the goal of developing targeted therapies for patients suffering from genetically defined cancers and metabolic diseases. Today, Biomea has grown to over 100 employees and built a management team with significant experience in precision oncology and in progressing products from early-stage research to clinical trials and ultimately to regulatory approval and commercialization. Biomea has built in-house expertise in medicinal chemistry, biology, translational medicine, computational biology, and chemistry, in vitro and in vivo pharmacology, biomarker development, and manufacturing. We have also established internal expertise in clinical development, clinical operations, pharmacovigilance, clinical pharmacology, regulatory, and quality control. Members of the management team have held various positions at several renown biotech companies, including Genentech, Gilead Sciences, Pharmacyclics, AbbVie, Celera and others. We are supported by our board of directors, scientific advisory board, and a leading syndicate of investors.

Our Programs

We believe that covalent small molecules have the potential to address the key limitations of existing reversible therapeutics and to treat diseases where targeted therapies are not yet approved. While as an organization we have not yet obtained approval to commercialize any of our product candidates and our management's past experience, including development of the covalent small molecule BTK inhibitor ibrutinib, does not guarantee similar results or success for our company, we believe such experience of our management team makes us well-positioned to address this opportunity and is a key competitive advantage. The following table summarizes our wholly owned research and development pipeline:



Biomea's current pipeline and potentially addressable patient population

BMF-219

Our lead product candidate, BMF-219, is designed to be an oral, potent, and selective covalent inhibitor of menin, a ubiquitously expressed scaffold protein that impacts multiple cellular processes including cell cycle control, apoptosis, and DNA damage repair[1]. Preclinical studies of BMF-219 have shown sustained potent abrogation of menin-dependent signaling and pathway control in vitro, ex vivo and in vivo. BMF-219 demonstrated consistent on-target inhibition with a strong anti-proliferative effect on various menin-dependent acute myeloid leukemia (AML) cell lines[2]; diffuse large B-cell lymphoma (DLBCL) cell lines representing categories of double/triple hit lymphoma (DHL/THL) and double expressor lymphoma (DEL)[3]; chronic lymphocytic leukemia (CLL) ex vivo models[2]; and multiple myeloma (MM) cell lines harboring diverse mutational backgrounds, including MYC dysregulation[4]. BMF-219 also exhibited high potency in in-vitro and ex-vivo KRAS-

[1] Agarwal SK, et al. *Horm Metab Res* 2005. DOI: 10.1055/s-2005-870139
[2] Somanath, P., Lu, D., Law, B. et al. Preclinical activity of irreversible Menin inhibitor, BMF-219, in chronic lymphocytic leukemia. JCO 2022; 40 (Supplement 16): 7541. DOI: 10.1200/JCO.2022.40.16_suppl.7541
[3] Somanath, P., Lu, D., Law, B. et al. Novel Irreversible Menin Inhibitor, BMF-219, Shows Potent Single Agent Activity in Clinically Relevant DLBCL Cells. Blood 2021; 138 (Supplement 1): 431
[4] Somanath, P., Lu, D., Law, B., et al. Anti-tumor activity of irreversible menin inhibitor, BMF-219, in high-grade B-cell lymphoma and multiple myeloma preclinical models. *Cancer Res* (2022) 82 (12_Supplement): 2654.

driven cancer cell models[5]. MYC, which exerts much of its oncogenic activity through interaction with menin, is a major downstream effector of the KRAS pathway[6]. In addition, we explored BMF-219 in two preclinical animal models of diabetes and observed strong, prolonged glycemic control, insulin sensitization, and HbA1c reduction[7,8].

BMF-219 Oncology Programs

BMF-219 is a covalent menin inhibitor being developed for the treatment of cancers that are highly dependent on menin. Currently we are enrolling COVALENT-101, 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 (NCT05153330). 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. We have also initiated and are enrolling COVALENT 102, a Phase 1 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).

BMF-219 Diabetes Program

Loss of functional beta cell mass is a core component of the natural history in both types of diabetes — type 1 diabetes (mediated by autoimmune dysfunction) and type 2 diabetes (mediated by metabolic dysfunction). Beta cells are found in the pancreas and are responsible for the synthesis and secretion of insulin, a hormone that helps regulate the body's capacity to absorb, metabolize, and convert glucose for energy. In patients with diabetes, beta cell mass and function are diminished, leading to insufficient insulin secretion and hyperglycemia. Menin is thought to act as a brake on beta cell turnover / beta cell growth, supporting the notion that inhibition of menin could lead to the regeneration of normal healthy beta cells. Based on these and other scientific findings, Biomea is exploring the potential for menin inhibition as a viable therapeutic approach to improve beta cell health and mass, and thus potentially treat an underlying driver of diabetes. We are currently enrolling the Phase II portion of COVALENT-111, a multi-site, randomized, double-blind, placebo-controlled Phase I/II study (NCT05731544). In the completed Phase I portion of the trial, healthy subjects were enrolled in single ascending dose cohorts to ensure safety at the prospective dosing levels for type 2 diabetic patients. Phase II consists of multiple ascending dose cohorts and includes adult patients with type 2 diabetes uncontrolled by current therapies.

BMF-500

Our second development candidate, BMF-500, a novel third generation covalent inhibitor of FLT3, 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

[5] Law, B., Lu, D., Somanath, P., et al. Irreversible menin inhibitor, BMF-219, inhibits the growth of KRAS-mutated solid tumors. *Cancer Res* (2022) 82 (12_Supplement): 2665.
[6] Chester E. Chamberlain, et al. Menin Determines K-RAS Proliferative Outputs in Endocrine Cells. J Clin Invest. 2014;124(9):4093-4101. https://doi.org/10.1172/JCI69004.
[7] Somanath, P., Mourya, S., Li, W., et al. Oral menin inhibitor, BMF-219, displays a significant and durable reduction in HbA1c in a type 2 diabetes rat model. EASD 2022 Short Oral Discussion (#590). https://www.abstractsonline.com/pp8/#!/10613/presentation/1318
[8] Butler, T., Mourya, S., Li, W., et al. Oral long-acting menin inhibitor normalises type 2 diabetes in two rat models. EASD 2022 Oral Presentation (#197). https://www.abstractsonline.com/pp8/#!/10613/presentation/934

to have a therapeutic profile to allow for combinations with standard of care and/or novel targeted agents like BMF-219.

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[9] . 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 BMF-219[10]. These data provide preclinical evidence for combining pathway-specific inhibitors as a promising therapeutic strategy for further investigation in acute leukemia. We announced the clearance of our IND for BMF-500 in the first half of 2023 and have initiated COVALENT-103 a Phase 1 clinical trial of BMF-500 in patients with acute leukemia (NCT05918692).

Additional Programs

We are currently advancing additional preclinical covalent small molecule programs for the treatment of select cancers. Our third development candidate is expected to be nominated soon. All these programs will pursue novel protein targets that should have single agent activity and also have the potential to achieve a synergistic anti-tumor effect when combined with one another.

Our Strategy

Our goal is to discover and develop a pipeline of novel covalent small molecules to treat patients with genetically defined cancers and metabolic diseases. The key elements of our business strategy to achieve this goal include:

- Deploy our covalent platform against high-value drivers of disease;
- Advance our product candidates to the clinic and through clinical development to maximize their potential benefit to patients;
- Continue to expand our portfolio of covalent small molecule product candidates;
- Evaluate opportunities to enhance the potential of our programs in collaboration with third parties;
- Maintain our entrepreneurial outlook, scientifically rigorous approach, and culture of tireless commitment to patients.

Key Advantages of Covalent Drugs

Since the discovery of aspirin in 1899, drugs that form permanent bonds with their target (covalent drugs) have been known to offer a number of potential safety, tolerability and efficacy advantages over conventional reversible drugs through multiple mechanisms, including:

- High selectivity: Covalent drugs have the potential to confer high selectivity to a target by interacting with the unique surrounding structural elements of the protein and establishing a covalent bond to a key residue in the binding site. Leveraging non-covalent and covalent interactions can lead to greater selectivity versus reversible compounds, which rely solely on non-covalent binding. This has the potential to reduce the likelihood of non-specific, off-target interactions that often lead to safety and tolerability concerns.

[9] Law, B., Rughwani, T., Archer, T., et al. Bmf-500: An Orally Bioavailable Covalent Inhibitor of FLT3 with High Selectivity and Potent Antileukemic Activity in FLT3-Mutated AML. Blood (2022) 140 (Supplement 1): 6191–6192. https://doi.org/10.1182/blood-2022-170445

[10] Law, B., Lu, D., Somanath, P., et al. Combinatorial approach using covalent menin inhibitor, BMF-219, and/or covalent FLT3 inhibitor, BMF-500, with MEK or BCL2 blockade potentiates therapeutic use in AML. Cancer Res (2023) 83 (7_Supplement): 4939. https://doi.org/10.1158/1538-7445.AM2023-4939

- Deep inactivation of target: Upon binding, a covalent inhibitor may not only cause inactivation of the target but may also result in the elimination of the target through normal cellular degradation processes. The diseased cell then either undergoes rapid apoptosis or differentiation into a normal, mature cell. Such transformation has the potential to provide the patient with a durable, lasting benefit.
- Greater therapeutic window: Covalent inhibitors are designed to create a permanent bond with high affinity and long residence time. Unlike conventional reversible drugs, which typically need to be present at higher concentrations 24/7 to provide benefit, covalent drugs have the potential to maintain their effect in the absence of sustained drug exposure. The permanent inhibition of target function upon covalent binding essentially uncouples pharmacodynamics (drug effects) (PD) from pharmacokinetics (drug exposure) (PK) as target inhibition persists after the drug has been cleared from the system. This property of covalent drugs can potentially lead to lower drug doses, less frequent dosing regimens, and better safety versus reversible approaches.

Our FUSION™ System Discovery Platform

We believe that covalent small molecules have the potential to address the key limitations of existing reversible therapeutics and treat diseases where targeted therapies are not yet approved. Leveraging our extensive experience developing covalent drugs and covalent binding chemistry expertise, we built our proprietary FUSION™ System to enable the design and development of novel covalent small molecule product candidates. Our FUSION™ System discovery platform encompasses the following:

- **Target Selection Validation and AI/VR Matching**: We use our expertise in structural biology and covalent binding chemistry to identify both validated and novel targets that we believe may have a demonstrable and specific impact on disease and have particular structural characteristics that would be amenable to direct intervention with a covalent binder.
- **Custom Scaffold Creation:** We create novel chemical scaffolds using a computational platform to exploit the unique structural elements of a specific target protein. We then screen these scaffolds with in-house technologies to select the optimal candidates for further construction and design. This evaluation process is intended to increase the probability of having multiple targeted compounds that can advance through the discovery process and into the clinic.
- **Molecule Optimization/Refinement:** Using our proprietary suite of computational technologies, assays, analytical approaches, chemistry, and know-how we strive to maximize the potential selectivity, potency, safety, and convenience of our oral, covalent small molecule product candidates. We avoid compound library screening, which ensures highly selective/specified scaffolds and saves considerable time during the lead optimization step. Further, this approach helps to ensure the creation of novel chemical matter that has a strong IP position.