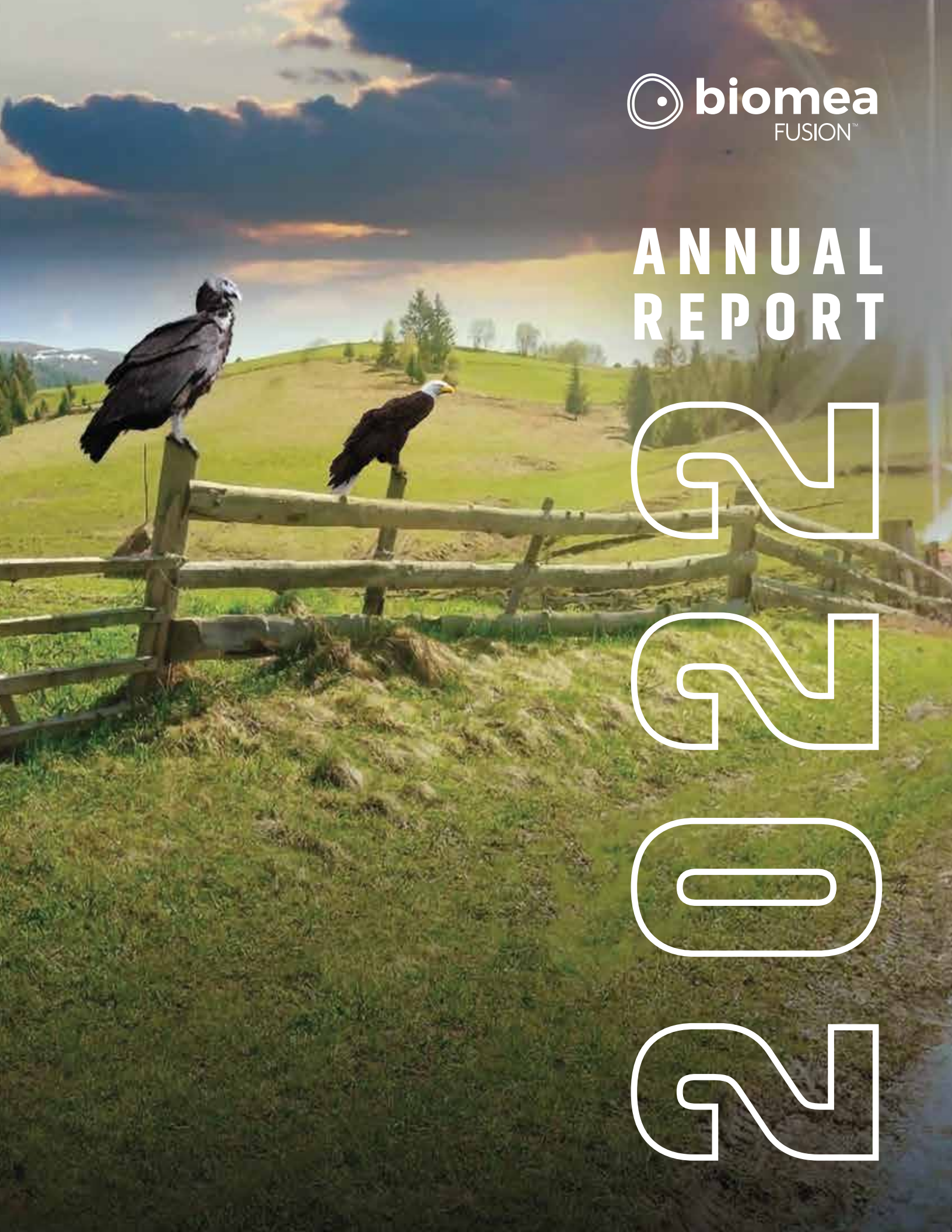
biomea
FUSION™
ANNUAL
REPORT
2020

DEAR SHAREHOLDERS, FRIENDS AND COLLEAGUES,

The company entered 2022 with big plans for BMF-219, an investigational small-molecule, covalent inhibitor of menin. The previous year was one of incredible growth, both in headcount and capital resources, which we need in order to properly execute our vision. With our first IND clearance under our belt and officially a clinical-stage company, the execution of our first clinical trial, COVALENT-101, and the expansion of our pipeline were at the forefront of our efforts. We expanded COVALENT-101 to include a total of four blood cancers, Acute Leukemia, Multiple Myeloma Diffuse Large B-Cell Lymphoma, and Chronic Lymphocytic Leukemia. Based on our pre-clinical work, we believe that BMF-219 has a unique ability to disrupt the continued growth and survival of these oncogenic immune cells. We also believe that BMF-219 has the potential to disrupt the growth and survival of KRAS-driven solid tumors, which supported the filing of the company's second IND application — and the second one for BMF-219. COVALENT-102, which dosed the study's first patient in January 2023, is enrolling patients with KRAS-mutated Non-Small Cell Lung Cancer, Colorectal Cancer, and Pancreatic Cancer. We filed our third IND for BMF-219 at the end of 2022 to support COVALENT-111, a Phase 1/2 for the treatment of Type 2 Diabetes Mellitus. We weren't quite done with the pipeline expansion effort and also announced in 2022 our second internally designed investigational covalent inhibitor, BMF-500, a small molecule targeting FLT3 for the treatment of Acute Myeloid Leukemia.

Our Mission, "We Aim to Cure," serves as our guiding light, which complements our vision to create breakthrough medicine that is tailored to the patient's need. We believe we can successfully achieve our goal by addressing the root cause of the patient's disease and by creating novel-novel combinations of unique mechanisms of action.
These novel-novel combinations would be tailored based on the driving force behind the particular cancer or metabolic disorder.

Team Fusion spent 2022 in its entirety setting up multiple study cohorts and clinical trials for BMF-219, as well as creating a second novel covalent inhibitor, which will now provide us with multiple clinical data readouts in 2023 and beyond. Despite the industry headwinds, we believe that strong clinical data and the evidence of innovation continues to be appreciated by investors and large pharma. Our ability to continue to optimize and leverage the Biomea FUSION SYSTEM™ to design novel and highly selective covalent inhibitors gives us the potential to create additional clinical opportunities in the near future.

I am pleased to share with you that in March 2023, we announced our first clinical readout for the company and the first for BMF-219. The readout covered the first two dosing cohorts of BMF-219 from the COVALENT-111 study, a double-blinded, randomized, placebo-controlled Phase 1/2 clinical trial investigating the effect of BMF-219 on patients who have uncontrolled Type 2 Diabetes Mellitus despite maintaining standard of care therapy. The data highlighted BMF-219's ability to lower patients' blood sugar levels as well as patients' HbA1C levels after just four weeks of therapy. The data was well-received, enabling the company to raise net proceeds of approximately $162 million at $30 per share.

Looking forward to the remainder of 2023, we anticipate Q2 will have a similar cadence as Q1, where we will announce new data from COVALENT-111 during the American Diabetes Association Annual Meeting in June. We also expect to announce our first clinical readout for COVALENT-101 in Cohort 1, which is enrolling relapsed/refractory Acute Leukemia patients. And finally, we anticipate filing an IND application for our second internally designed covalent inhibitor, BMF-500, by the end of June. Lots of exciting developments are coming up.

Biomea Fusion, and hence TEAM FUSION, is comprised of a *group of highly skilled, adaptable, and dedicated problem solvers that are hungry for the next challenge, next target, the next pinnacle (think of Everest, Denali, etc.) — (*group of **B**rilliant, **I**nnovative, and **O**ptimistic **M**asters who **E**nlighten those around them to **A**dapt to the challenges ahead.)

I couldn't be more proud of TEAM FUSION (!) with their tireless effort, coupled with sheer speed, to enable the company to execute at such a high level. We believe with continued execution, we will reach our goal, our long game, as "We Aim to Cure."

I am glad you are joining us on this very exciting journey.

BEST REGARDS,

- Thomas Butler,
CEO and Chairman of the Board of Biomea Fusion, Inc.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-40335

Biomea Fusion, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**82-2520134**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
900 Middlefield Road, 4th Floor Redwood City, California	**94063**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 980-9099

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value	BMEA	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Market on June 30, 2022, was $255,911,000.

The number of shares of Registrant's Common Stock outstanding as of March 21, 2023 was 29,608,622.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, on or before the date 120 days after the conclusion of the Registrant's fiscal year ended December 31, 2022 pursuant to Regulation 14A in connection with the Registrant's 2023 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

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Special Note Regarding Forward Looking Statements

This Annual Report on Form 10-K contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our financial performance;
- the sufficiency of our existing cash, cash equivalents and investments to fund our future operating expenses and capital expenditure requirements;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our anticipated use of our existing cash, cash equivalents and investments;
- the implementation of our strategic plans for our business and product candidates;
- the size of the market opportunity for our product candidates and our ability to maximize those opportunities;
- the initiation, timing, progress and results of our research and development programs, preclinical studies, clinical trials and investigational new drug applications (INDs) and other regulatory submissions;
- the beneficial characteristics, safety, efficacy and therapeutic effects of our product candidates and the ability of our FUSION™ System to generate additional product candidates with such characteristics;
- the timing, progress and focus of our ongoing and future clinical trials, and the reporting of data from those trials;
- the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other favorable results;
- our plans relating to the clinical development of our product candidates, including the disease areas to be evaluated;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our plans relating to commercializing our product candidates, if approved;
- our estimates of the patient populations addressable by our product candidates, if approved, and the number of participants that will enroll in our ongoing and planned clinical trials;
- the expected benefits of potential future strategic collaborations with third parties and our ability to attract collaborators with development, regulatory and commercialization expertise;
- the success of competing therapies that are or may become available;
- the timing or likelihood of regulatory filings and approvals, including our expectation to seek special designations, such as orphan drug designation, for our product candidates;
- our plans relating to the further development and manufacturing of our product candidates, including for additional indications that we may pursue;
- existing regulations and regulatory developments in the United States and other jurisdictions;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available;
- our plan to rely on third parties to conduct and support preclinical and clinical development;
- our ability to retain the continued service of our key personnel and to identify, hire and then retain additional qualified personnel;

- the impact of the ongoing COVID-19 pandemic or other related disruptions on our business;
- unfavorable global economic conditions, including inflationary pressures, market volatility, acts of war and civil and political unrest; and
- our expectations regarding the period during which we will qualify as an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended.

We have based these forward-looking statements largely on our current expectations, estimates, forecasts and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the section titled "Risk Factors" for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. We qualify all of the forward-looking statements in this Annual Report on Form 10-K by these cautionary statements.

Summary Risk Factors

The following is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address every aspect of our risks factors, all of the risks that we face, or other factors not presently known to us or that we currently believe are immaterial. Additional discussion of the risks summarized in these summary risk factors, and other risks that we face, can be found under the heading "Risk Factors" in this Annual Report on Form 10-K and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the Securities and Exchange Commission, or SEC, before making investment decisions regarding our common stock.

- We have a limited operating history, have not completed any clinical trials, have no products approved for commercial sale, and have not generated any revenue, which may make it difficult for you to evaluate our current business and likelihood of success and viability.
- We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and product development programs or future commercialization efforts.
- Our discovery and preclinical development is focused on the development of novel covalent small-molecule therapies to treat patients with genetically-defined cancers and metabolic diseases, and the approach we are taking to discover and develop such binders is novel, may never lead to marketable products and may not ultimately represent a significant market.
- Our novel approach to the discovery and development of our current and future product candidates is unproven, and we may not be successful in our efforts to use and expand our FUSION System to build a pipeline of product candidates with commercial value.
- We are very early in our development efforts and are substantially dependent on our lead product candidate, BMF-219. If we are unable to advance BMF-219, BMF-500 or any of our future product candidates through clinical development, obtain regulatory approval and ultimately commercialize BMF-219, BMF-500 or any of our future product candidates, or experience significant delays in doing so, our business, financial condition and results of operations will be materially adversely affected.
- Preclinical and clinical drug development is a lengthy and expensive process, with an uncertain outcome. Our preclinical and clinical programs may experience delays or may never be initiated or completed, which would adversely affect our ability to obtain regulatory approvals or commercialize our product candidates on a timely basis or at all, which could have an adverse effect on our business.

- The results of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or other comparable foreign regulatory authorities. Successful preclinical studies and clinical trials cannot provide assurance of successful commercialization.
- We have no experience as a company in conducting clinical trials.
- The ongoing COVID-19 pandemic and adverse global economic conditions, including supply chain issues and inflationary pressures, could materially adversely impact our business, results of operations, and financial condition, including our preclinical studies and clinical trials.
- The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.
- The price of our stock may be volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company 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 an orally bioavailable, potent and selective covalent inhibitor of menin, built from our FUSION System. We currently have clinical studies of BMF-219 underway in patients with liquid and solid tumors, as well as patients with type 2 diabetes. Menin is an important transcriptional regulator known to play a direct role in oncogenic signaling in multiple cancers and in beta cell homeostasis. Menin also serves as a checkpoint to prevent beta cell proliferation. Thus, we believe inhibiting menin via BMF-219 has the potential to enable the proliferation, preservation, and reactivation of healthy, function beta cells capable of producing insulin, thereby leading to long-term glycemic control in patients with type 2 diabetes.

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, normalizing glucose levels during treatment and even after drug washout. As of December 31, 2022, BMF-219 is being evaluated in up to eight liquid and solid tumor types and in type 2 diabetes across three ongoing clinical trials.

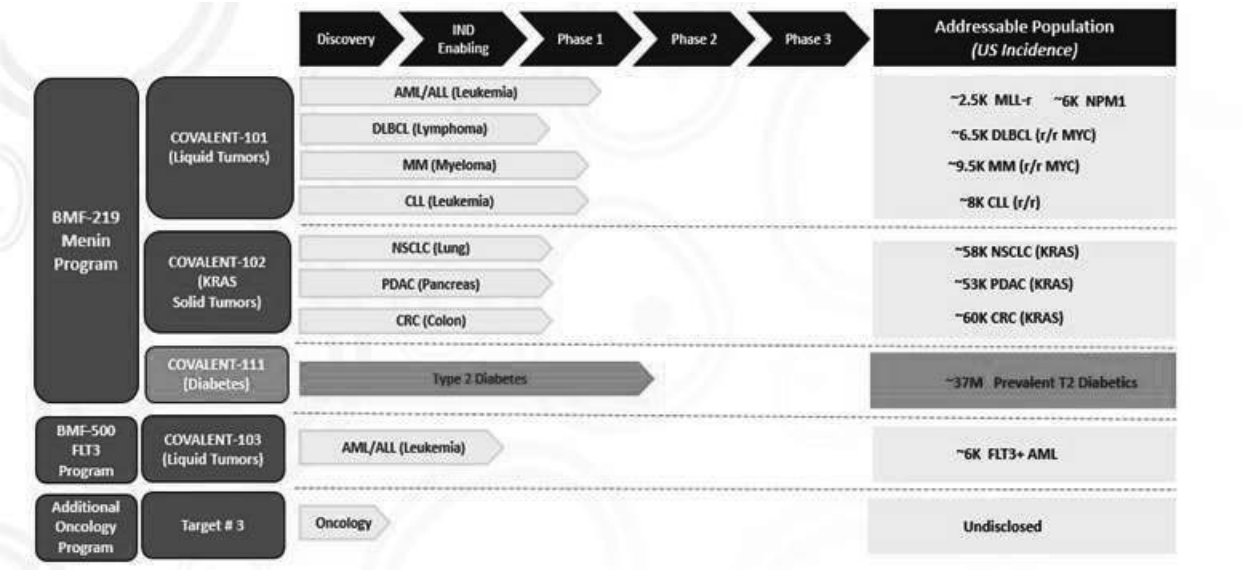
Beyond BMF-219, we are utilizing our novel FUSION System to pioneer covalent treatments against other high-value genetic drivers of disease. In May 2022, we announced the nomination of our second development candidate, BMF-500, a covalent inhibitor of FLT3, and presented preclinical data on this program in December 2022. We expect to file an Investigational New Drug application (IND) with the U.S. Food and Drug Administration (FDA) to study BMF-500 in acute leukemias in the first half of 2023.

We are currently advancing additional preclinical covalent programs for the treatment of select diseases and expect to nominate our third development candidate in the first half of 2023. Our goal is to utilize our capabilities and FUSION System platform to become the leader in developing covalent small molecules to maximize the depth and durability of clinical benefit when treating various diseases.

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, Inc. (the "Company" or "Biomea") in 2017 with the goal of developing targeted covalent therapies for patients suffering from diseases with a high unmet medical need. Our management team has significant experience in multiple disease areas, including precision oncology and in progressing products from early-stage research to clinical trials and ultimately to regulatory approval and commercialization. Together, they bring 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. Our management team members have held various leadership roles at Genentech, Gilead Sciences, Pharmacyclics and Celera. We are supported by our board of directors and our scientific advisory board.

Our Programs

We believe that covalent small molecules have the potential to address key limitations of existing reversible therapeutics and 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 team's past experience, including developing IMBRUVICA® (ibrutinib), does not guarantee similar results or success for Biomea, we believe such experience of our management team positions us well to deliver this opportunity for novel covalent small molecules and is a key competitive advantage. The following table summarizes our wholly owned research and development pipeline:



Our current pipeline and potentially addressable patient population

Our lead product candidate, BMF-219, is designed to be an orally bioavailable, potent, and selective covalent inhibitor of menin, a ubiquitously expressed scaffold protein that functions in histone modification and epigenetic gene regulation to impact multiple cellular processes including cell cycle control, apoptosis, and DNA damage repair.

We are developing BMF-219 for the treatment of menin dependent diseases such as subtypes of acute leukemia, KRAS solid tumors, and type 2 diabetes mellitus. Preclinical studies of BMF-219 have shown sustained potent abrogation of menin-dependent oncogenic 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; diffuse large B-cell lymphoma (DLBCL) cell lines representing categories of double/triple hit lymphoma (DHL/THL) and double expressor lymphoma (DEL); chronic lymphocytic leukemia (CLL) *ex vivo* models; and multiple myeloma (MM) cell lines harboring diverse mutational backgrounds, including MYC dysregulation. BMF-219 also exhibited high potency in *in vitro* and *ex vivo* KRAS-driven cancer cell models. MYC, which exerts much of its oncogenic activity through interaction with menin, is a major downstream effector of the KRAS pathway.

At medical conferences in 2021 and 2022, we presented several abstracts and posters on BMF-219's observed ability to alter MYC gene expression and genomic function in acute leukemia cells. We presented the pronounced cell lethality we observed with BMF-219 in two MYC-dependent DHL/DLBCL cell lines at the American Society of Hematology (ASH) Annual Meeting in 2021 and released additional preclinical data on the effect of BMF-219 in liquid and solid tumors in 2022 at American Association for Cancer Research (AACR), American Society for Clinical Oncology (ASCO), and International Myeloma Society (IMS).

In January 2022, we announced that we had initiated dosing in COVALENT-101, a Phase 1 clinical trial to explore the safety and efficacy of BMF-219 in patients with relapsed/refractory AML and acute lymphoblastic leukemia (ALL), including those with MLL/KMT2A gene arrangements or NPM1 mutations. In 2022, we amended the IND to initiate additional cohorts in the COVALENT-101 study to explore the potential utility of BMF-219 across a range of menin-dependent hematologic malignancies including MM, DLBCL, and CLL.

In October 2022, we announced the initiation of a Phase 1/1b clinical trial of BMF-219 (COVALENT-102) 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.

In January, June, and September of 2022 we released preclinical data on the observed effect of administration of BMF-219 in multiple animal models in diabetes. 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, we are exploring the potential for menin inhibition as a possible therapeutic approach to improve beta cell health and mass, and thus potentially treat an underlying driver of diabetes. In October 2022, we announced completion of the Phase 1 portion of COVALENT-111, a Phase 1/2 clinical trial of BMF-219 in healthy volunteers and adults with type 2 diabetes in Canada. In December 2022, we announced FDA clearance of the IND for BMF-219 in type 2 diabetes, allowing us to expand the COVALENT-111 study to sites in the United States. In January 2023, we announced the dosing of the first patient with type 2 diabetes in the United States.

Beyond BMF-219, we are utilizing our novel FUSION System to pioneer covalent treatments against other high-value genetic drivers of disease. In May 2022, we announced the nomination of our second development candidate, BMF-500, a third-generation covalent inhibitor of FLT3, which demonstrated picomolar IC50 values across key FLT3 isoforms, potentially making it the most potent inhibitor of its class. Activating mutations of the FMS-like tyrosine kinase 3 (FLT3) are the most frequent genetic alteration in AML and are associated with poor prognosis. We expect to file an IND to study BMF-500 in acute leukemias in the first half of 2023.

At the ASH Annual Meeting in December 2022, we presented BMF-500's picomolar affinity to activating FLT3 mutations including FLT3 internal tandem duplications (FLT3-ITD) and various tyrosine kinase domain (TKD) mutations, multi-fold higher potency and increased cytotoxicity than commercially available non-covalent FLT3 inhibitor gilteritinib, and complete tumor regression at physiologically relevant doses in mouse models of FLT3-ITD AML and maintenance of effect without continued exposure. BMF-500 selectively killed AML cells harboring FLT3 activating mutations, including MV4-11 and MOLM-13, and engineered cells expressing FLT3-ITD and/or FLT3 TKD mutations. In *ex vivo* cultures, BMF-500 as a single agent induced potent growth inhibition of patient-derived AML cells harboring either FLT3-ITD or FLT3 non-ITD mutations.

We are currently advancing additional preclinical covalent small molecule programs for the treatment of select cancers and expect to nominate our third development candidate in the first half of 2023. 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 BMF-219.

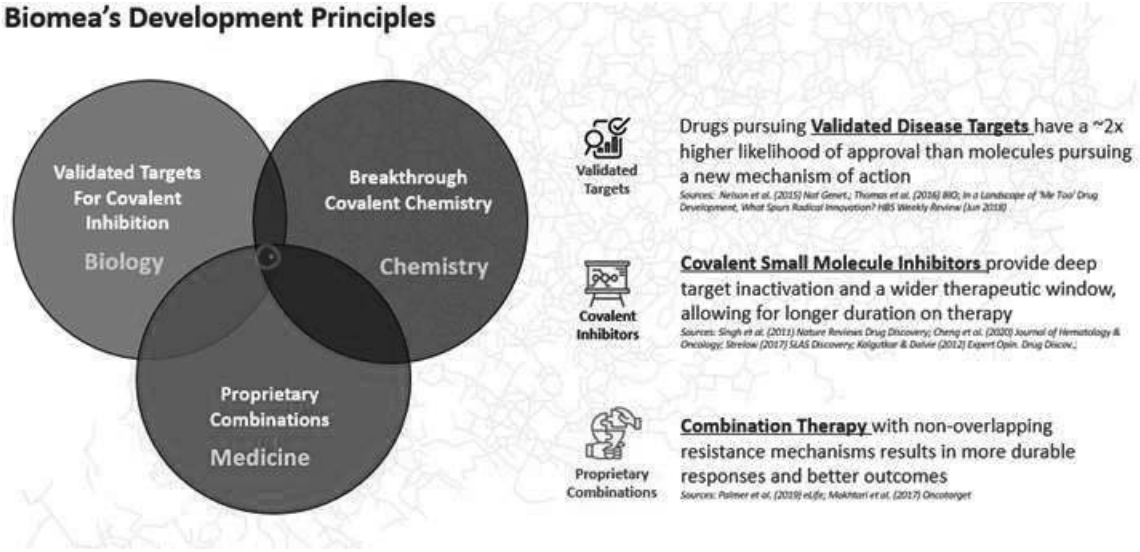
Our Strategy – We Aim to Cure

Our scientists have identified a series of molecular targets whose role in healthy individuals is to function quietly and efficiently, keeping this equilibrium largely undisturbed. In cancer, these proteins malfunction, thus disrupting their complex biochemical pathways, resulting in abnormal cell growth and division. When the body's own defense mechanisms are unable to restore the healthy equilibrium, tumors and late-stage disease occur. In these tumors, the rogue proteins continue to be expressed above their normal levels. We recognize the value of precision, targeting the malfunctioning proteins through quick-acting inhibition.

Our scientists, with extensive backgrounds in structure-driven drug discovery and development, have taken aim at these molecular targets using covalent inhibition techniques. Most commercial drugs and clinical-stage drug candidates rely exclusively on keeping bloodstream levels at a sufficiently high amount to which the patient is constantly exposed. The patient is thus subject to unwanted side effects caused by the drug's potentially indiscriminate activity against other targets that are not themselves out of equilibrium. In contrast, our approach specifically employs weak spots in the molecular target that can form a covalent or extremely tight bond with the drug, but in such a way that the inhibitor-protein complex is then taken out of action quickly. The only way then for the rogue protein to return is through de novo synthesis. This allows the drug to be dosed in short bursts, to do its job, and then disappear instead of having to be always present. While perhaps

counterintuitive, we believe this approach affords an added degree of selectivity, since "innocent" targets are not exposed to the drug for any longer than necessary.

With a wealth of experience in delivering versatile, multibillion dollar covalent inhibitor drugs such as IMBRUVICA (ibrutinib), we believe our team is uniquely positioned to leverage this knowledge in wide variety of unmet medical needs.



Biomea aims to combine expertise in biology, chemistry, and medicine to create a suite of novel agents to improve and extend life for patients

The key elements of our business strategy include:

- **Deploy our covalent platform against high-value oncogenic drivers of cancer.** Leveraging our extensive experience developing covalent drugs and our structural biology and covalent binding chemistry expertise, we built our proprietary FUSION System to design and develop a pipeline of novel covalent small molecule product candidates. We believe covalent binders offer a number of potential advantages over conventional reversible drugs, including greater target selectivity and the ability to drive deeper, more durable responses with lower drug exposure. Our goal is to utilize our capabilities and platform to become a leader in developing covalent drugs.
- **Continue to advance our lead product candidate, BMF-219, through clinical development.** BMF-219 is a covalent menin inhibitor being developed for the treatment of cancers that are highly dependent on menin, including leukemias containing the mixed-lineage leukemia (MLL) fusion protein. In January 2022, we announced that we had dosed the first patient in our first-in-human Phase 1 clinical trial of BMF-219 (COVALENT-101) in patients with relapsed or refractory acute leukemia and have subsequently expanded the trial to enroll cohorts of patients with relapsed/refractory (R/R) MM, DLBCL, and CLL. We are also studying BMF-219 across a range of menin dependent solid tumors including KRAS mutant lung, pancreatic, and colon tumors in the ongoing Phase 1/1b COVALENT-102 trial. Beyond cancer, we are exploring the potential of BMF-219, to treat type 2 diabetes in the ongoing Phase 1/2 COVALENT-111 trial.
- **Continue to expand our portfolio of covalent small molecule product candidates.** In addition to BMF-219, we are advancing two other preclinical covalent programs for the treatment of select cancers and announced our second development candidate, BMF-500, a covalent FLT3 inhibitor in May 2022. We expect to nominate our third development candidate in the first half of 2023. Both of these preclinical programs target clinically validated mechanisms of action and are complementary to the menin pathway.
- **Evaluate opportunities to enhance the potential of our programs in collaboration with third parties.** We own full worldwide development and commercialization rights to each of our programs. In the future, we may selectively enter into collaborations where we believe there is an opportunity to speed up clinical development or enhance the commercialization potential of our product candidates. We intend to commercialize our product candidates in key markets either alone or with partners in order to maximize the worldwide commercial potential of our programs.
- **Maintain our entrepreneurial outlook, scientifically rigorous approach, and culture of tireless commitment to patients**. We will continue to apply transformative science in the development of novel targeted therapies for

patients suffering from cancers with limited therapeutic options. We intend to continue building our team of qualified individuals who share our commitment to collaboration and scientific rigor in the development of novel covalent product candidates that may have the potential to treat patients with genetically defined cancers and metabolic diseases.

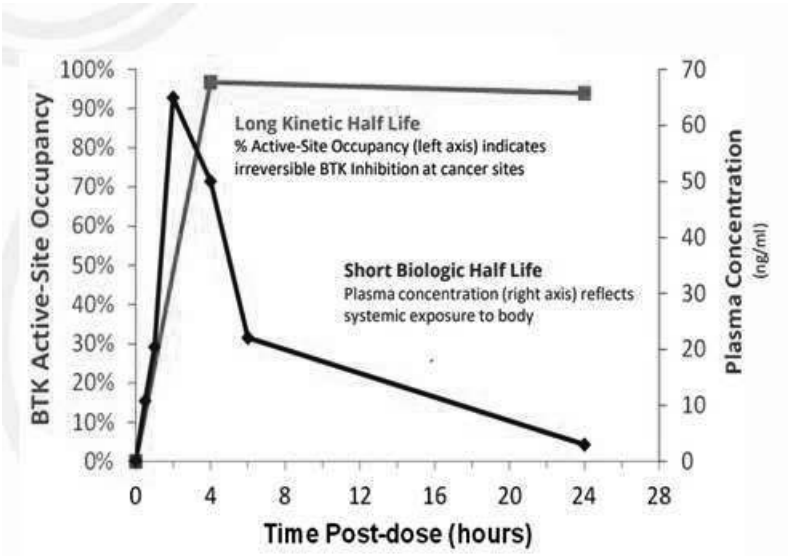
Background on Covalent Inhibition

A covalent small molecule drug is a synthetic compound that forms a permanent bond to its target protein through a combination of non-covalent and covalent interactions and can either stimulate or inhibit target protein function. Reversible drugs, which make up the majority of approved drugs, exert their action by establishing an equilibrium between free drug, target protein, and drug-target complex. Therefore, a reversible inhibitor, by definition, can allow an inhibited drug-protein complex to convert back to free drug and active protein unless sufficient concentration of free drug is present in the local environment. This need for constant coverage typically requires continuous systemic exposure, which can pose safety and tolerability challenges.

Forming a covalent bond between a target protein and covalent drug can be described as a two-step process. First, the compound creates a reversible, non-covalent bond to the target protein that can enable a covalent bond by placing a reactive atom on the drug compound close to a complementary reactive atom on the target protein. The second step involves the formation of a specific and long-lived covalent bond between the complementary moieties, resulting in a complex that persists throughout the lifetime of the target protein and effectively permanently disables target protein function.

Key Advantages of Covalent Drugs

Since the discovery of aspirin in 1899, covalent drugs have shown the potential to offer a number of potential safety, tolerability, and efficacy advantages over conventional reversible drugs through multiple mechanisms.



Persistent site occupancy of a marketed, covalent inhibitor in the absence of sustained drug exposure

Beyond aspirin and ibrutinib, a number of covalent inhibitors have been approved by the FDA, including sofosbuvir (marketed as SOVALDI® for hepatitis C virus), tenofovir (marketed as VIREAD® for hepatitis B virus), osimertinib (marketed as TAGRISSO® for NSCLC), and bortezomib (marketed as VELCADE® for MM and mantle cell lymphoma).

Challenges in Developing Covalent Drugs

Despite the potential advantages of covalent drugs, the majority of approved drugs are reversible binders. The inherent challenges in creating covalent drugs present significant barriers to entry to discover and develop these molecules. The key challenges in developing covalent drugs include:

- **Complexity.** The discovery and development of covalent drugs requires significant structural knowledge and medicinal chemistry capabilities, including the ability to construct complex novel chemical scaffolds. In addition, not all disease-causing proteins have the properties necessary for the application of covalent binding. While advancements in structural knowledge of the proteome provides greater opportunity to identify potential targets for

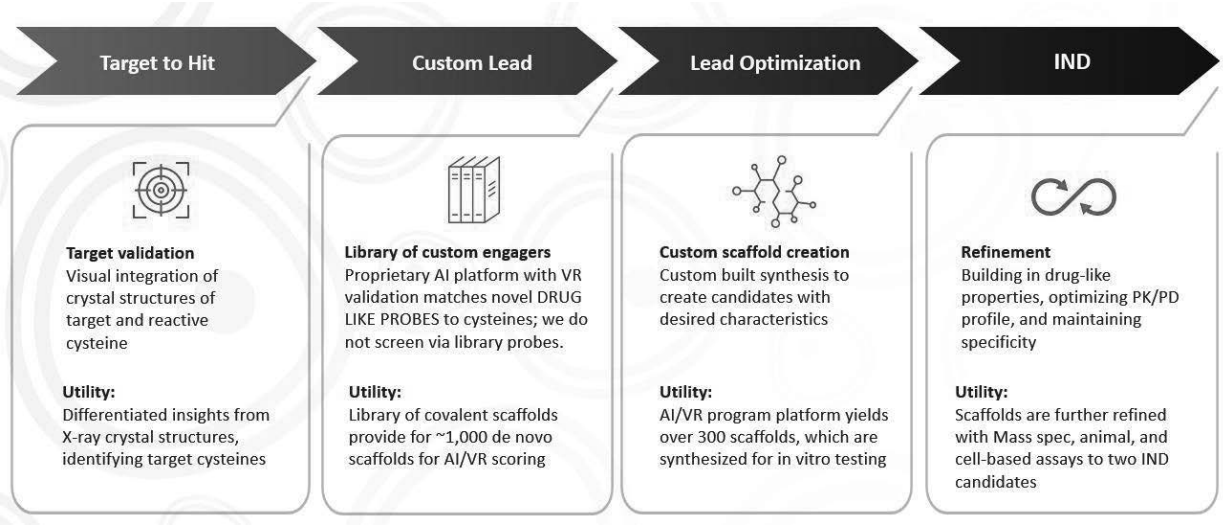
covalent binding, we believe the lack of specialized medicinal chemistry expertise needed to leverage this knowledge has impeded the development of covalent drugs.

- **Safety and toxicity.** While the covalent binding modality can provide a high degree of selectivity, poorly conceived molecules with promiscuous binding profiles can pose a risk of significant off-target interactions and safety concerns. Given this significant and long-standing challenge, without the structural biology and covalent binding chemistry expertise, drug developers have historically been discouraged from pursuing covalent binders.

At Biomea, we believe we are positioned to leverage the significant expertise, foundational knowledge, and capabilities that our management team first acquired while developing ibrutinib and that we have expanded and refined over the last three years to create our FUSION System discovery platform.

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 against high-value oncogenic drivers of cancer. The system also has the capability to create a novel non-covalent inhibitor, which we may advance depending on the target. We have described some of the differences between the FUSION System and traditional small molecule drug discovery approaches below:



The FUSION System leverages AI/VR matching and custom synthesis to develop novel drugs

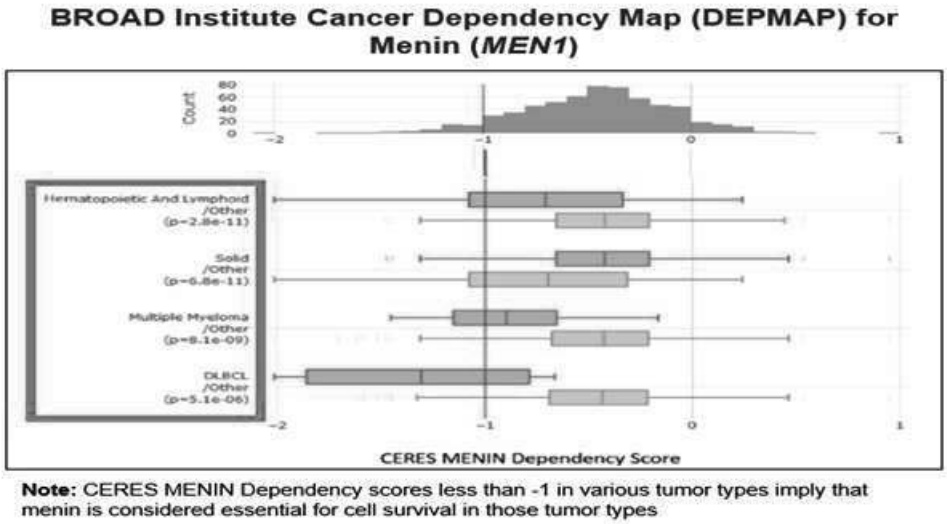
Our FUSION System discovery platform encompasses the following:

- **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 results in highly selective/specified scaffolds. This saves considerable time during the lead optimization step.

We aim to leverage our capabilities and platform to establish ourselves as a leader in developing covalent small molecules in order to maximize the depth and durability of clinical benefit for patients with various cancers and metabolic diseases.

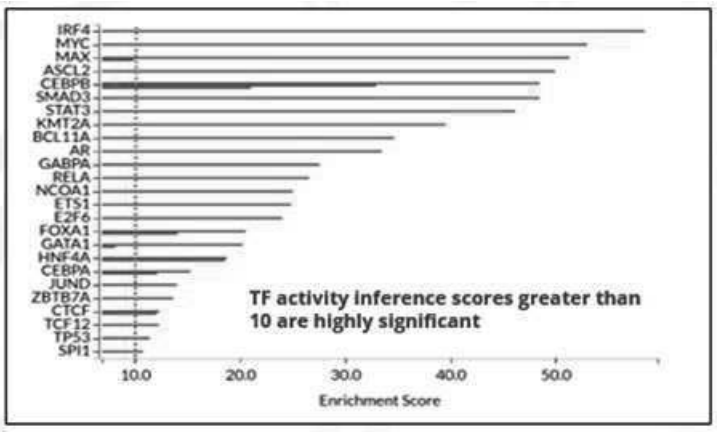
Our Initial Focus: Menin

Menin is a protein important to transcriptional regulation, impacting major processes such as cell cycle control, apoptosis and DNA damage repair. It plays an essential role in oncogenic signaling in subgroups of genetically defined leukemias, such as MLL-r, and other cancers dependent on menin. Inhibition of menin is a novel approach to cancer treatment.
The BROAD Institute elucidated the dependence of menin on various cancer types and has made this work available for public access via the DEPMAP portal. The dependence of various cancers on menin is shown in the figure below. Cell viability scores have shown that menin plays a key role in survival of multiple tumors. High menin dependency in liquid and solid tumors, beyond acute leukemias, provides rationale for further analysis in dependent tumor types. Biomea is clinically exploring the potential for covalent inhibition of menin in a variety of liquid and solid tumor types.



BROAD Institute DEPMAP highlights the dependency of various tumor types on menin (MEN1)

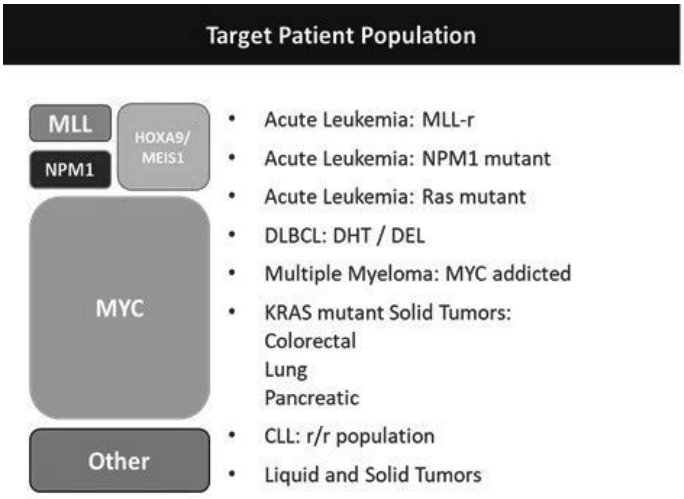
As shown above, DLBCL; MM; Hematopoietic and Lymphoid Tumors (including Acute Leukemias); and Solid Tumors (KRAS mutant) had the highest dependence on menin. We believe that disrupting the function of menin in these tumor types is a viable therapeutic approach. The menin complex plays a critical role in MYC-dependent oncogenic signaling, whereby menin enhances MYC-mediated transcription to promote cancer progression.



TF activity interference using chip-seq of differentially expressed genes in MOLM-13 cells incubated with 500 nM BMF-219 at 24 hours. Each bar represents a study in the GEO repository using the specified TF antibody

In MOLM-13 cells treated with BMF-219, the top transcription factors regulating gene expression were MYC and its cofactor MAX. IRF4, MYC, and MAX are known drivers for some forms of DLBCL, (addicted) multiple myeloma, and multiple additional tumors.

Inhibition of menin is a novel approach to cancer treatment. The figure below highlights the menin complex partner / downstream effector that is associated with each of the respective indications that could benefit from treatment with a covalent menin inhibitor.

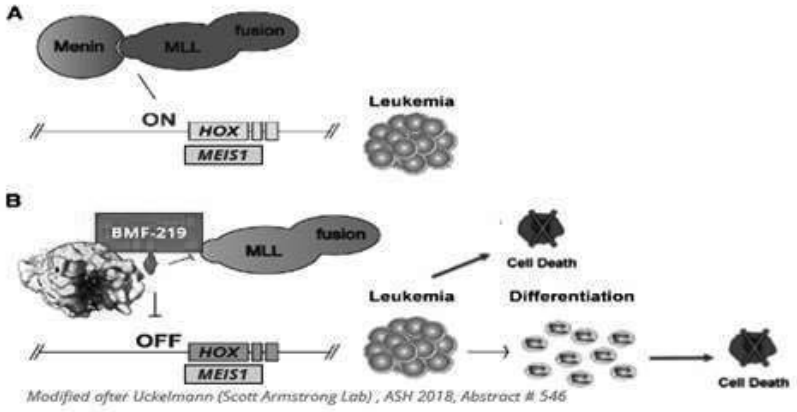


Depiction of target patient populations grouped based on the relevant menin complex partner or downstream effector

Menin & MLL – Acute Leukemias (MLL-r and NPM1 Mutant)

MLL-r leukemias are characterized by MLL gene (encoded by the gene *KMT2A*) translocation abnormalities. These abnormalities result in the formation of fusion genes encoding fusion proteins comprised of MLL1 and a corresponding fusion partner domain. The interaction of these fusion proteins with menin drives the expression of downstream target genes such as *HOXA9* and *MEIS1*, triggering leukemic cell proliferation.

Menin binds directly to the conserved N-terminus of MLL proteins, making it a promising target that could potentially be exploited consistently by a menin inhibitor therapeutic. Preventing the MLL proteins from binding to menin has been shown to abolish the oncogenic effects *in vitro* and *in vivo* as shown in the figure below.



Depiction of leukemic pathway associated with aberrant menin-MLL fusion complex

Approximately 20,000 and 6,000 patients in the United States are diagnosed annually with AML and ALL, respectively. MLL-r leukemia has limited therapeutic options and represents approximately 10% of acute leukemias in adults and approximately 70% of acute leukemias in infants. In addition to MLL-r, MLL signaling in some forms of MLL wild-type (MLL-wt) AML have also been implicated, including those bearing independent oncogenic mutations in nucleophosmin (NPM1), a molecular chaperone, and DNA-methyltransferase 3A (DNMT3A), a methyl transferase. These subpopulations together represent approximately 45% of AML cases.

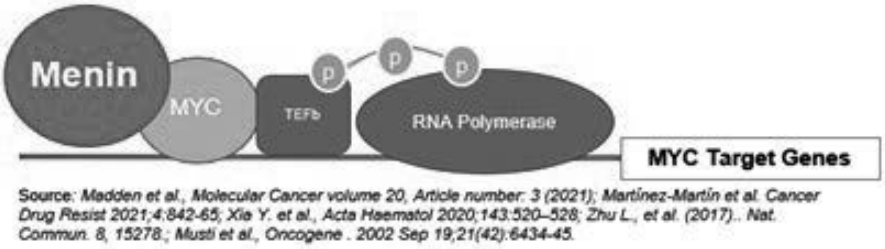
Patients with MLL rearrangements often suffer from failure of induction therapy or disease relapse, resulting in poor clinical outcomes. In pediatric AML, the five-year event-free survival rate on average is 44% but ranges between 11% and 92% depending on the MLL-translocation subtypes. In ALL, the five-year survival rate for people aged 20 and older is approximately 40% and for people under the age of 20 it is approximately 89%. However, pediatric MLL-r ALL patients fare much worse, with four-year survival rates as low as 10%, compared to 64% for those without MLL rearrangements.

A perhaps more dire area of unmet need is relapsed/refractory AML. Despite evolving insights into the pathogenesis of AML, over 11,000 patients with AML die each year from the disease in the United States. Relapse is the most common cause of treatment failure. The five-year overall survival (OS) for adult patients with AML after disease relapse is only approximately 10%. Furthermore, a published study showed that approximately 20% of patients demonstrated primary induction failure adding even more patients to this refractory category. Currently, allogeneic hematopoietic cell transplantation (HCT) is considered to be the only reliable option with curative potential, with OS estimated between 15% to 25% three to five years post-transplant. To improve overall quality of life for patients, physicians are favoring oral targeted agents and strategies that avoid intensive chemotherapy and prolonged inpatient admissions. Key in this effort is a focus on molecular testing to identify the potential for targeted therapies.

Given the involvement of MLL and NPM1 in a high percentage of acute leukemias, and the poor clinical outcomes provided by available treatments, we believe a new treatment that can inhibit the function of both targets by disrupting or preventing interactions with menin could address this unmet need.

Menin & MYC – DLBCL, MM, CLL and KRAS Solid Tumors (Lung, Pancreatic, and Colorectal)

MYC is a transcription factor that is implicated in oncogenesis and typically regulates genes associated with cell cycle, cellular proliferation, differentiation, and apoptosis. In fact, MYC is constitutively and aberrantly expressed in over 70% of human cancers. Notably, MYC appears to play a key role in the functioning of many cancer cells, including DLBCL, MM, and KRAS solid tumors (Colorectal, Pancreatic, and Lung). MYC is aberrantly expressed or translocated in relapsed / refractory DLBCL and MM and is a major downstream effector of KRAS mutant tumors. Menin has been shown to play an essential role in the MYC transcriptional complex, which leads to menin-mediated enhancement of MYC target gene expression in cancer cells. The figure below highlights the role of menin in mediating MYC target gene expression.



Source: Madden et al., Molecular Cancer volume 20, Article number: 3 (2021); Martínez-Martín et al. Cancer Drug Resist 2021;4:842-65; Xia Y. et al., Acta Haematol 2020;143:520–528; Zhu L., et al. (2017).. Nat. Commun. 8, 15278.; Musti et al., Oncogene . 2002 Sep 19;21(42):6434-45.

The role of menin in the MYC transcriptional complex, facilitating the expression of MYC target genes

DLBCL is the most common subtype of Non-Hodgkin Lymphoma. DLBCL starts in white blood cells called lymphocytes and it usually grows in lymph nodes. Every year, approximately 18,000 people in the U.S. are diagnosed with DLBCL. Following initial treatment with standard chemotherapy, approximately 70% of patients have a complete response and approximately 50% of patients are cured. There is a substantial unmet need for patients with relapsed or refractory DLBCL as median overall survival is between six and seven months in this group. Double Hit Lymphomas (DHL), Triple Hit Lymphomas (THL), and Double Expressor Lymphomas (DEL) are high grade B-cell lymphomas (HGBLs) that have high MYC and BCL2 or BCL6 dependency. Based on their aggressive nature, DHL, THL, and DEL represent a large portion of the relapsed or refractory DLBCL population.

MM is a cancer of plasma cells, which make antibodies (immunoglobulins) and are mainly located in the bone marrow. As cancerous cells migrate from the bone marrow, organ damage due to excess immunoglobulins in bones and blood and weakening of bones are common features. Approximately 35,000 people in the U.S. are diagnosed with MM each year and the five-year relative survival rate is approximately 56% (Source: NCI SEER Data). While many therapeutic options are available to patients, a subset of highly refractory patients exists. In these patients, overall survival is as low as 6 months. Additionally, it is estimated that more than 60% of MM patients have menin dependent genetic drivers (MYC addicted or driven) and that these drivers are more common in the relapsed or refractory setting.

CLL is a chronic leukemia that progresses relatively slowly and typically impacts older adults. In the United States, approximately 20,000 patients are diagnosed with CLL each year. CLL is a disease of malignant B lymphocytes, for which standard-of-care agents are generally well tolerated; however, CLL patients with certain genetic backgrounds demonstrate inferior outcomes to these regimens. While the existing treatments options produce 5-year survival outcomes greater than 87%, there is an unmet need for patients that have high- or medium-risk cytogenetic profiles and those that are relapsed or refractory to existing treatments.

Non-Small Cell Lung Cancer (NSCLC) is the most common form of lung cancer, representing approximately 84% of all lung cancer cases or approximately 200,000 cases in the U.S. each year. Additionally, the five-year survival rate of NSCLC is approximately 26%. While lung cancer is the third most common form of cancer in the U.S. based on incidence, lung cancer contributes to the highest number of annual cancer deaths in the U.S. KRAS is a key node in the RAS signaling pathway, which can be oncogenic. KRAS is the most frequent oncogene in NSCLC, occurring in approximately 30% of patients with NSCLC. Notably, RAS signaling is known to result in active MYC, which can facilitate pro-tumor transcriptional processes. KRAS-targeted inhibitors have shown efficacy in KRAS mutant NSCLC patients in clinical trials.

Pancreatic cancer is a relatively rare form of cancer in the U.S., representing approximately 60,000 cases in the U.S. each year. Pancreatic cancer is an aggressive cancer with a very low five-year survival rate of approximately 11%, indicating that there is a large unmet need. It is rarely diagnosed early, contributing to the low survival rate. Among patients with pancreatic cancer, RAS mutations (including KRAS) occur in up to approximately 98% of patients.

Colorectal cancer is the fourth most common form of cancer in the U.S., representing approximately 150,000 cases in the U.S. each year. These cancers start in the rectum or the colon and can be diagnosed/identified early, even potentially as noncancerous polyps. The five-year survival rate of CRC is approximately 65%. Among other mutations, KRAS mutations occur in approximately 40% of patients with CRC.

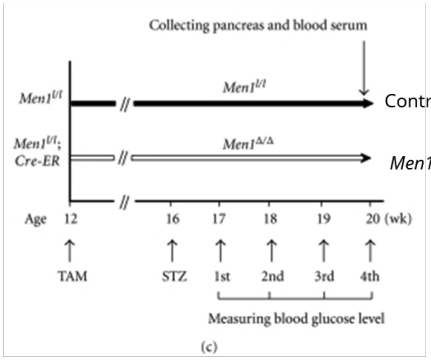
Menin & Beta-Cell Biology – Diabetes

Diabetes mellitus is characterized by a reduced ability to produce insulin and/or by a dysregulated response to insulin and affects approximately 37 million people in the U.S. (Source: CDC). Diabetes is one of the largest economic burdens on the U.S. health care system and the 7th leading cause of death in the U.S. According to the CDC, worldwide 537 million adults have diabetes. In the United States alone, 37.3 million Americans have diabetes, 11.3% of the population. 96 million adults (more than 1 in 3) in the U.S. have pre-diabetes. In the United States, $1 out of every $4 in U.S. health care costs is being spent on caring for people with diabetes. In 2021, the U.S. spent $380 billion to treat diabetes. Today, diabetes is an uncontrolled disease despite the availability of current medication. There is a significant need for the treatment and care of diabetes patients.

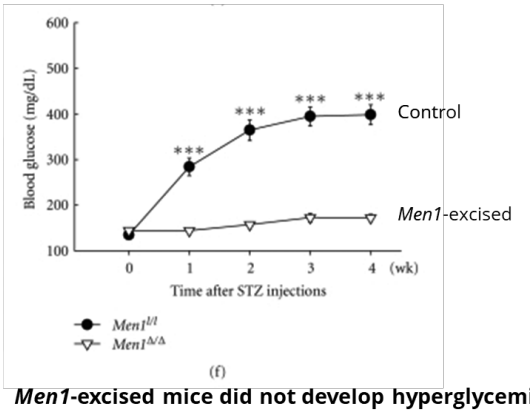
Diabetes is grouped into a few clinical categories based on etiology or timing of diagnosis according to the latest guidance from the American Diabetes Association (ADA). Accounting for 1.6 million diagnosed patients in the U.S., type 1 diabetes is due to autoimmune beta cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood. Type 2 diabetes has been diagnosed in approximately 25.3 million people in the U.S. and is due to a progressive loss of adequate beta cell insulin secretion frequently on the background of insulin resistance. The primary treatment goal is to achieve glycemic control by reducing HbA1c (A1c), a marker for the amount of sugar in the bloodstream, to 6.5% or lower. Glycemic control is a validated approach to delaying disease progression, which leads to significant and potentially fatal renal, cardiac, neurological, and ophthalmic comorbidities.

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. Insulin is a hormone that helps the body use glucose for energy and helps control blood glucose levels. 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. Notably, it has previously been shown that knocking out the gene responsible for the creation of menin (*MEN1*) has been observed to produce profound glycemic control in diabetic animal models (see below). Based on these and other scientific findings, we are exploring the potential for menin inhibition as a viable therapeutic approach to permanently halt or reverse progression of type 2 diabetes.

MEN1 Excision Prevents Development of Streptozotocin (STZ)-induced Hyperglycemia



Multiple low-dose streptozotocin (MLD-STZ) administered to the control and *Men1*-excised mice to induce beta cell damage and a diabetes-like environment



***Men1*-excised mice did not develop hyperglycemia in STZ model, which was observed in the control group**

Sources: Yang et al. (2010) Deletion of the Men1Gene Prevents Streptozotocin-Induced Hyperglycemia in Mice. Experimental Diabetes Research, 2010, 1–11. doi:10.1155/2010/876701

MEN1 knockdown led to profound glycemic control in a streptozotocin-induced hyperglycemia mouse model

BMF-219 in Oncology

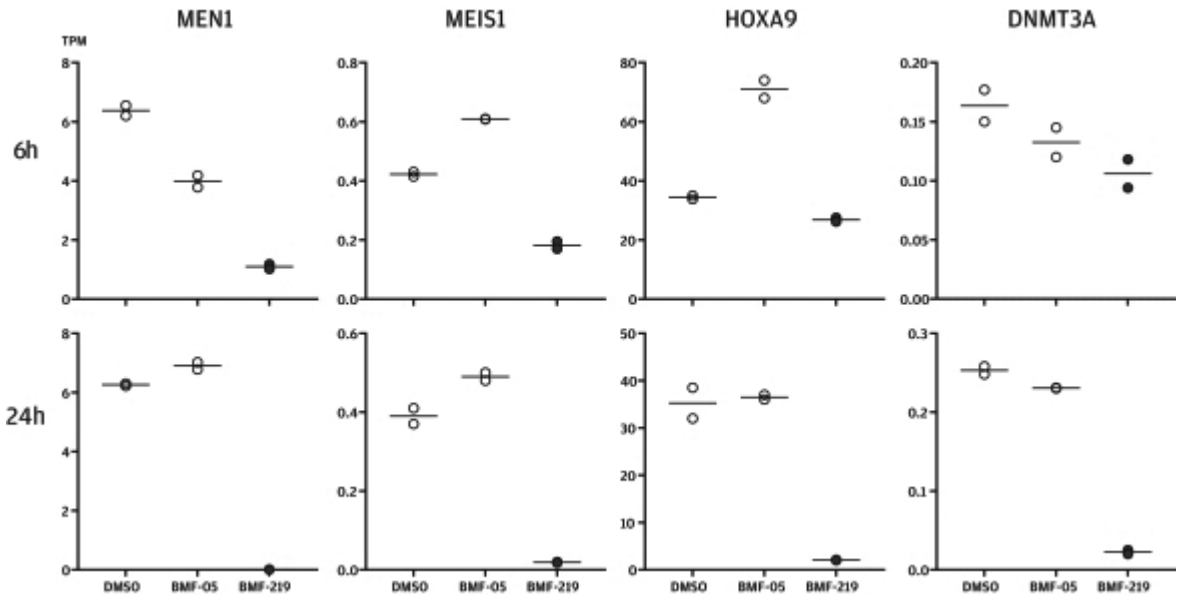
Our lead product candidate, BMF-219, is designed to be a potent, selective, orally bioavailable, covalent inhibitor of menin that disrupts the protein-protein interaction between menin and MLL. We are developing BMF-219 for the treatment of cancers that are highly dependent on menin, including leukemias containing the MLL fusion protein. In preclinical studies, administration of BMF-219 has resulted in robust anti-tumor responses across a range of liquid and solid tumor models, including MLL-r AML, NPM1 mutant AML, MYC driven/addicted liquid tumors (e.g., DLBCL and MM), and KRAS mutant colorectal, lung, and pancreatic tumors. Based on our preclinical findings, we believe our covalent approach may have significant advantages over reversible inhibitors, including selectivity, potency, durability, and safety.

Target Engagement Studies: Gene Expression

Published preclinical studies have shown that inhibition of the menin-MLL interaction leads to reduction in *MEN1* (the gene that encodes menin) transcription, resulting in down regulation of *MEIS1*, *HOXA9,* and *DMNT3A*, which are common gene signatures for menin-MLL, and differentiation of leukemic cells into myeloid cells. Our lead product candidate, BMF-219, is intended to irreversibly inhibit the interaction between menin and wild type MLL and MLL fusions.

In preclinical studies, administration of BMF-219 has resulted in the inhibition of the menin-MLL interaction in multiple cancer cell models with known dependency on menin binding for survival. We characterized the molecular responses following treatment with BMF-219 across multiple model cell lines, including MOLM-13 cells in culture. MOLM-13 is an AML cell line with a KMT2A-MLLT3 (MLL-AF9) fusion.

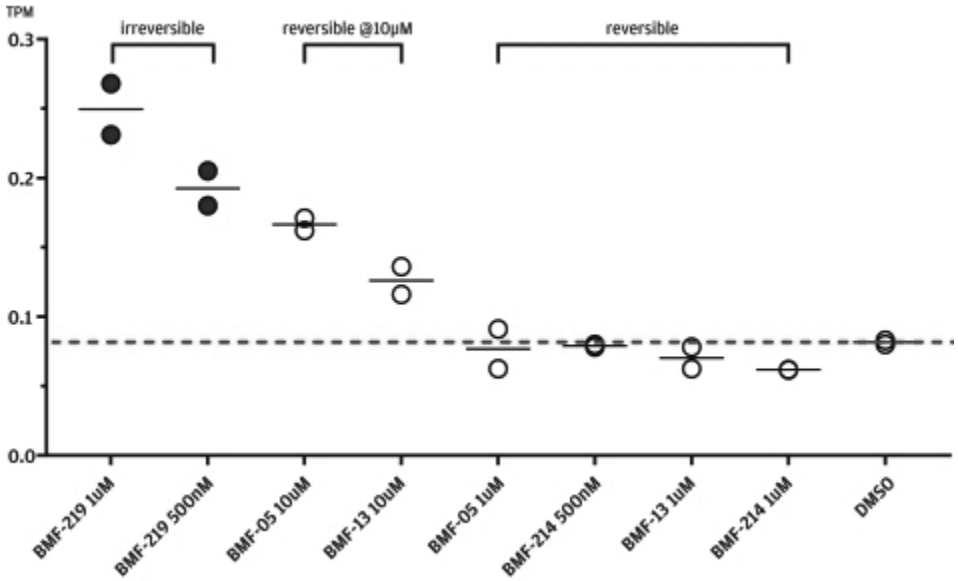
As reflected in the figure below, in this model we observed substantial down regulation of *MEN1* along with *MEIS1*, *HOXA9*, and *DNMT3A*, which are common gene signatures for menin-MLL and NPM1 altered leukemias. Published studies of reversible menin inhibitors have shown downregulation of signature genes after six days of inhibition. To evaluate target engagement and explore potential differences in onset of action for our reversible and covalent menin inhibitors, we evaluated expression levels at 6 and 24 hours following treatment. Our reversible inhibitor showed limited impact on signature genes over 24 hours, but we observed rapid down regulation of menin dependent genes for BMF-219 and observed up to approximately 80% reduction in readout genes by six hours and approximately 95% reduction at 24 hours compared to control.



Reduction in menin dependent gene expression demonstrated BMF-219 target engagement

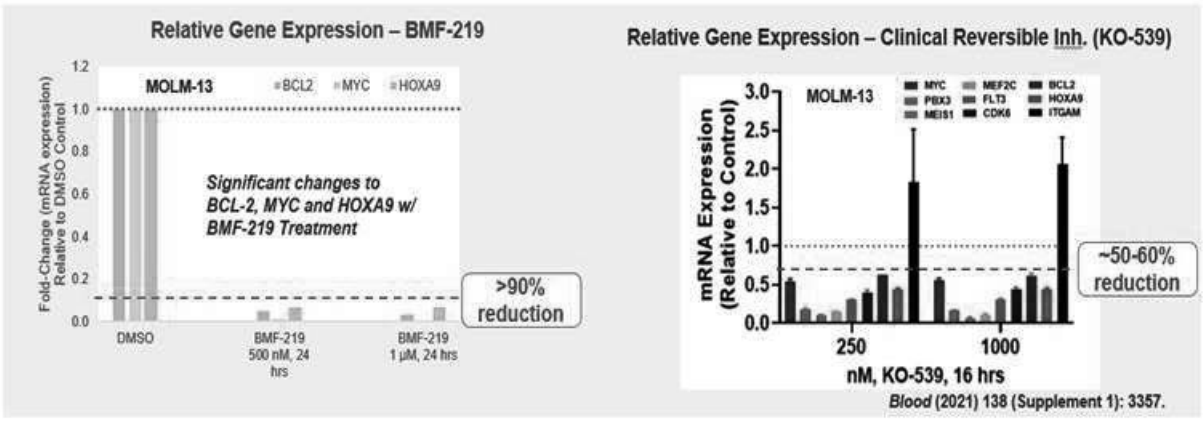
As reflected in the figure above, profiling of signature genes in menin-MLL and NPM1 altered leukemias showed rapid downregulation upon treatment with BMF-219, a covalent menin inhibitor. Treatment with BMF-05, a reversible menin inhibitor, showed limited impact on signature genes similar to dimethyl sulfoxide (DMSO) vehicle control at these time points, which is consistent with published findings for other reversible menin inhibitors. The Y-axis represents Transcripts Per Million (TPM).

Published preclinical studies have also shown that disruption of the menin-MLL interaction led to differentiation of leukemic cells to myeloid cells. As a result, we have tested reversible and covalent menin inhibitors in MOLM-13 cells to determine if treatment would promote differentiation, as exhibited by an increase in integrin subunit alpha M (*ITGAM*), which encodes CD11b, a surface marker associated with myeloid differentiation. As reflected in the figure below, at 24 hours following administration, we observed dose dependent elevation of myeloid marker gene expression with BMF-219 treatment. Meanwhile, comparable exposures of reversible menin inhibitors (BMF-05, BMF-13 and BMF-214, three of our proprietary reversible menin inhibitors) reflected no change from vehicle controls. However, the reversible inhibitors were able to upregulate ITGAM at a 10-fold increase in exposure. While we believe these results support our hypothesis regarding the role of the menin pathway, they also highlight the potential need for reversible inhibitors to have high clinical exposures in order to achieve sufficient menin suppression to affect disease.



Responses of myeloid differentiation marker ITGAM at 24 hours demonstrated target engagement. Y-axis represents the Transcripts Per Million (TPM). Data are presented for DMSO vehicle control, proprietary reversible menin inhibitors (BMF-05, BMF-13, BMF-214), and BMF-219

We explored the impact of BMF-219 treatment on key oncogenic genes in MOLM-13 cells in preclinical models. Significant changes in gene expression of BCL-2, MYC, and HOXA9 were observed after 24 hours of treatment with BMF-219. The figure below compares gene expression data in MOLM-13 cells after 16 hours of treatment with KO-539, a reversible menin inhibitor, that was published at the ASH Annual Meeting in 2021.

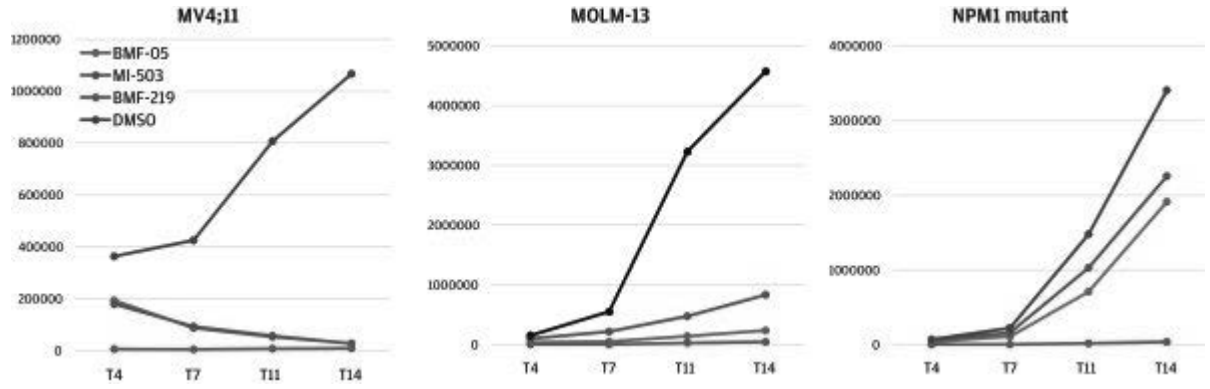


Comparison of gene expression data for key genes in MOLM-13 cells. Data for BMF-219 was gathered after 24 hours of BMF-219 treatment at 500 nM and 1,000 nM concentrations and was generated by the Biomea team. Data for KO-539 was gathered after 16 hours of KO-539 treatment at 250 nM and 1,000 nM concentrations and was generated by a research group at MD Anderson and subsequently published at the ASH Annual Meeting in 2021

In-vitro Studies

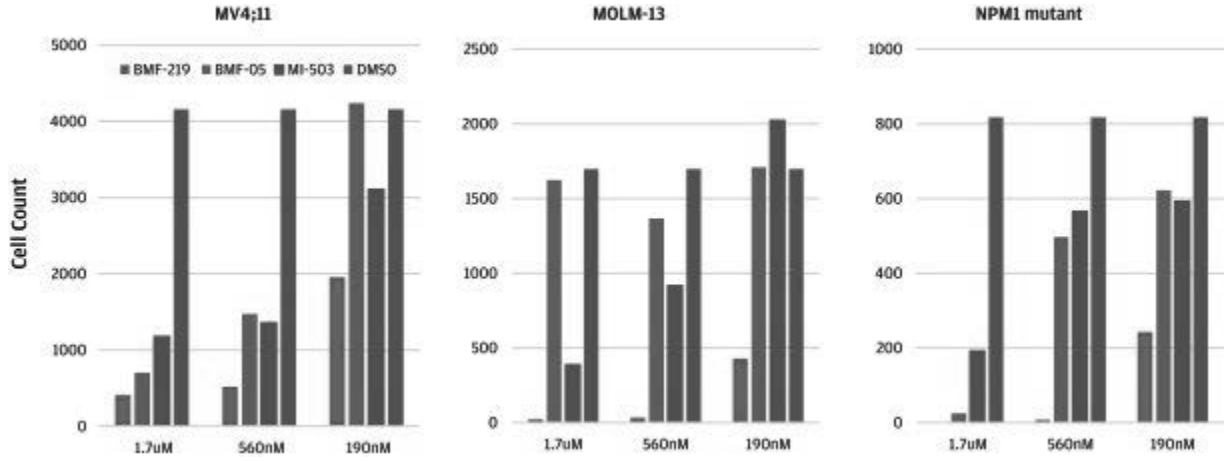
To evaluate potential activity of the covalent menin inhibitor BMF-219 in leukemia models, we examined the impact of menin inhibition on metabolic activity and cell survival. As reflected in the figures below, treatment with BMF-219 demonstrated rapid shut down of metabolic activity, which was sustained over the 14-hour study duration. BMF-219

responses were superior to tested reversible menin inhibitors (BMF-05 and MI-503) with respect to both onset and durability of metabolic suppression.



Metabolic activity in menin inhibitor treated leukemia cell lines reflected rapid and durable responses following administration of covalent menin inhibitor BMF-219 (560 nM exposure of all compounds). Y-axis represents fluorescence units measured as an output of ATP production, a measure of viable cells

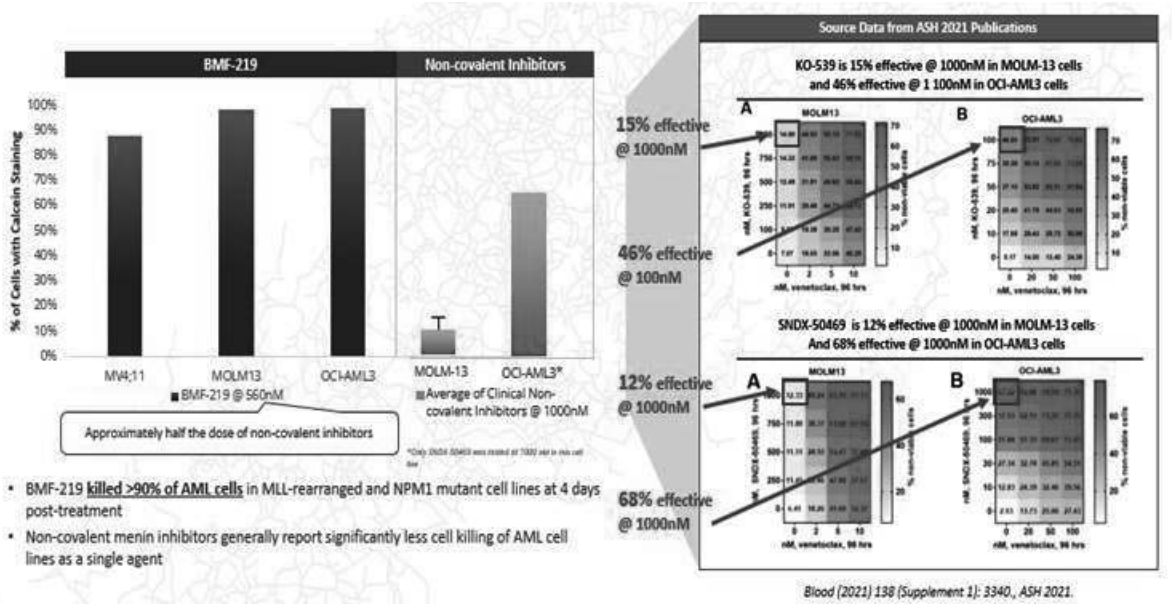
Treatment with BMF-219 also led to apoptosis in menin driven leukemia models, resulting in a notable reduction in cell survival. Responses were observed for BMF-219 treatment at the lowest tested doses across all cell lines, while the reversible inhibitors showed limited responses at the lowest dose and were unable to eliminate tumor cells at any tested dose.



Cell survival assay across AML cell lines after seven days shows differentiated responses to covalent menin inhibitor BMF-219 relative to reversible inhibitors

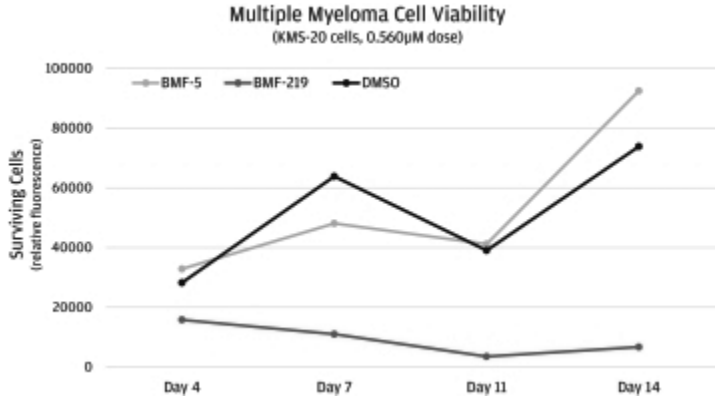
We also conducted cell proliferation assays on a panel of well-characterized leukemia cell lines to evaluate the potency of BMF-219. The panel included: MLL-AF4 translocated, internal tandem FLT3 duplicated bi-phenotypic B-myelomonocytic leukemia (i.e. ALL/AML) cell line MV4;11; MLL-AF9 translocated, internal tandem FLT3 duplicated AML cell line MOLM-13; and NPM1-mutated AML cell line OCI-AML3. We are comparing in the figure below the cell killing ability of BMF-219 in leukemic cells to the cell killing of reversible inhibitors in similar experiments. The data for reversible inhibitors

on the right of the figure was generated by a research group at MD Anderson and was published at the ASH Annual Meeting in 2021.



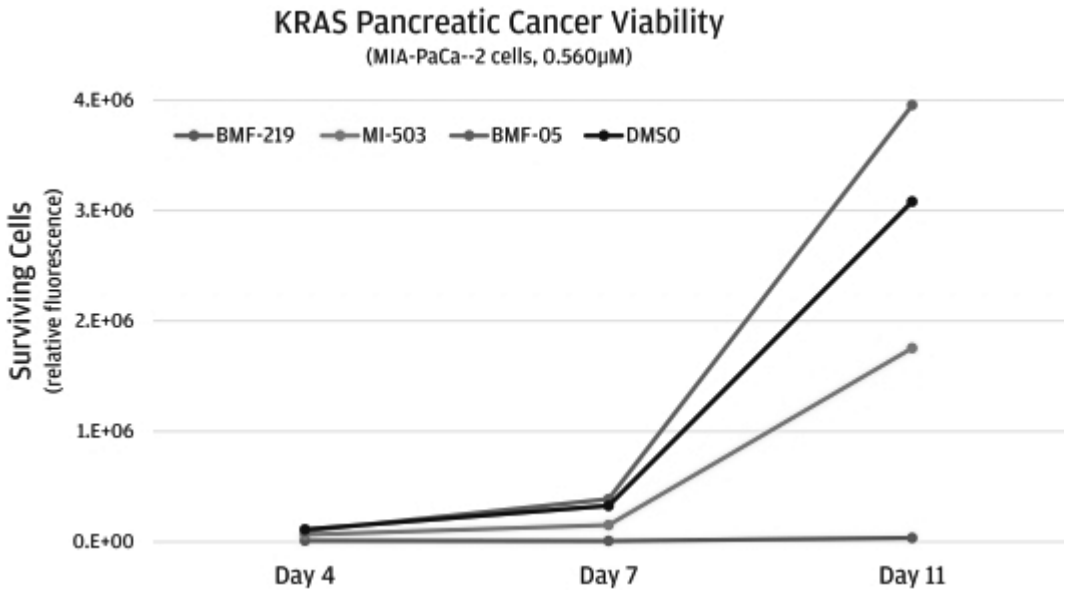
Cell killing effect of BMF-219 in acute leukemia cell lines compared against similar data from reversible menin inhibitors published at the ASH Annual Meeting in 2021

In addition to impacting leukemic cell lines, menin is a known dependency in other liquid tumors, including MM and DLBCL. Menin dependency has also been seen in multiple solid tumors including Ewing's sarcoma and KRAS driven cancers. As part of our ongoing discovery efforts, we screened BMF-219 against a panel of tumor models and observed potent growth inhibition in multiple menin-dependent cancer cell lines, including MM.



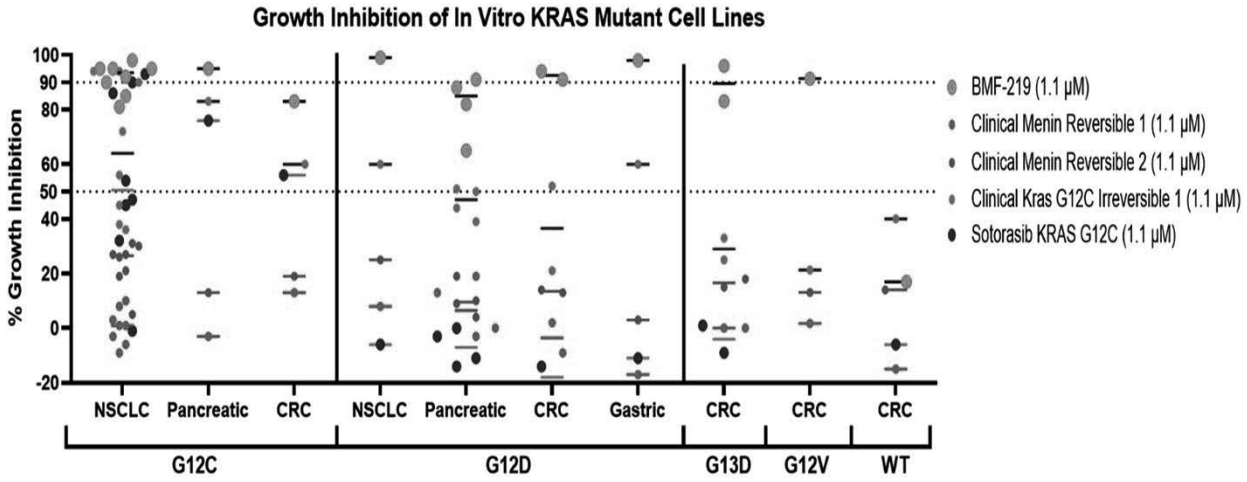
Representative cell survival time course from a multiple myeloma model (KMS-20 cell line, 0.56μM doses) shows relative effect of the covalent inhibitor BMF-219 versus a reversible inhibitor BMF-05

We also explored the potential potency of BMF-219 in KRAS dependent tumors using a long-term proliferation assay. A representative cell survival time course from a G12C KRAS mutation driven pancreatic cancer line (MIA-PaCa-2, 0.56 μM doses) shows the effects of treatment with the covalent inhibitor BMF-219. A broader panel of these studies demonstrated potent growth inhibition in multiple models covering both G12C and G12D KRAS mutations.



Representative cell survival time course from a KRAS mutant pancreatic cancer model (MIA-PaCa-2 cell line, 0.56µM doses) shows relative effect of the covalent inhibitor BMF-219 versus reversible inhibitors MI-503 and BMF-05

Single agent BMF-219 also showed strong and highly specific pan-KRAS anti-cancer activity as a single agent across KRAS G12C, G12D, G12V and G13D mutant cell lines including in NSCLC, CRC, and the most prevalent type of pancreatic cancer, PDAC. Across tested cell lines and KRAS mutations, BMF-219 produced higher growth inhibition compared to two approved KRAS G12C inhibitors as well as two clinical non-covalent menin inhibitors.



Growth inhibition effect of BMF-219 across KRAS G12C, G12D, G13D, and G12V mutant cell lines but not WT KRAS as presented at the AACR Annual Meeting in 2022, "Irreversible Menin Inhibitor, BMF-219, Exhibits Potent Cytotoxicity in KRAS-Mutated Solid Tumors" (Abstract 2665)

BMF-219 also demonstrated potent single agent activity across multiple preclinical models in DLBCL and MM. To measure cell killing, cells were cultured in the presence of menin inhibitor for 72 hours or 14 hours and viable cell count measure by CTG readout. The % cell killing relative to untreated cultures was measured at 72 hours and 14 hours. Data tabulated was averaged from two independent experiments.

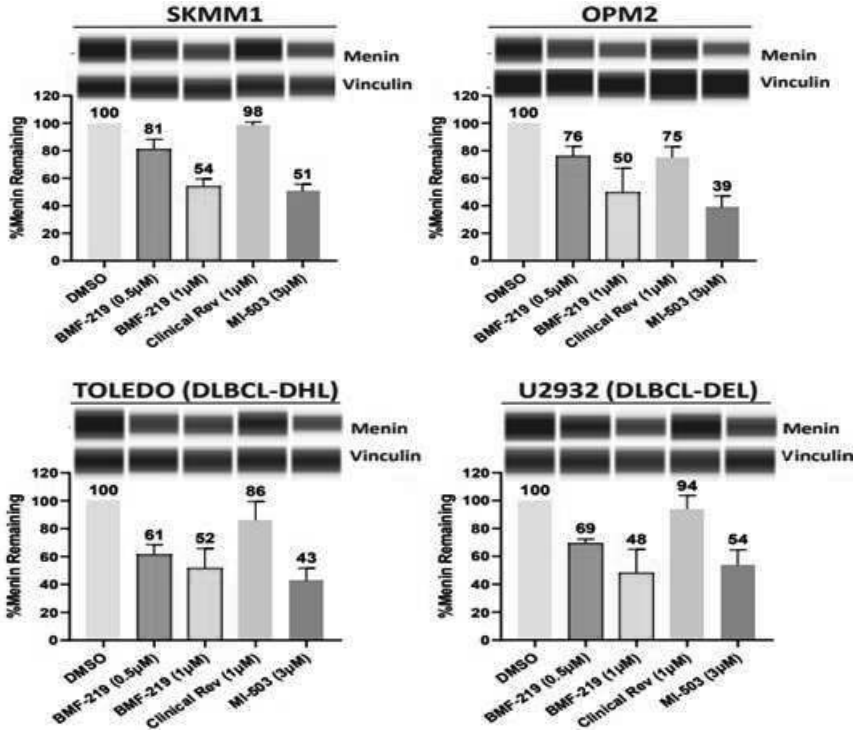
BMF-219 at 1µM induced potent killing with 80-97% cell death following 72 hours drug treatment. In comparison, the reversible menin inhibitors MI-503 and a clinical reversible menin inhibitor induced much less potent killing (20-35% cell killing with 3µM MI-503).

% Cell Death	SKMM1					OPM2				
	BMF-219			Clin Rev	MI-503	BMF-219			Clin Rev	MI-503
Conc.	0.4 µM	0.5 µM	1 µM	1 µM	3 µM	0.4 µM	0.5 µM	1 µM	1 µM	3 µM
14 hr	-	15	25	0	13	-	8	57	0	14
72 hr	27	-	86%	4	33	22	-	80%	3	21

% Cell Death	TOLEDO					U2932				
	BMF-219			Clin Rev	MI-503	BMF-219			Clin Rev	MI-503
Conc.	0.4 µM	0.5 µM	1 µM	1 µM	3 µM	0.4 µM	0.5 µM	1 µM	1 µM	3 µM
14 hr	-	18	12	0	11	-	19	36	0	7
72 hr	32	-	97%	0	35	29	-	86%	3	34

BMF-219 Exerted Potent Lethality Against Representative DLBCL (Toledo & U2932) & MM Cell Lines (SKMM1 & OPM2) as presented at the IMS Annual Meeting in 2022, "Anti-tumor Activity of Irreversible Menin Inhibitor, BMF-219, in High Grade B-Cell Lymphoma and Multiple Myeloma Preclinical Models" (Poster P-107)

BMF-219 was observed in preclinical studies to reduce menin protein in MM and DLBCL cells. Quantitation of menin protein expression in SKMM1, OPM2, Toledo and U2932 cell line treated with BMF-219, clinical reversible menin inhibitor or preclinical reversible menin inhibitor, MI-503, for 14 hours. Average menin protein expression is of three independent experiments. WES blot is a representative from one single experiment. Cells were cultured in the presence of menin inhibitors for 72 hours or 14 hours. Average % cell killing treated at 72 hours and 14 hours are from two independent experiments.



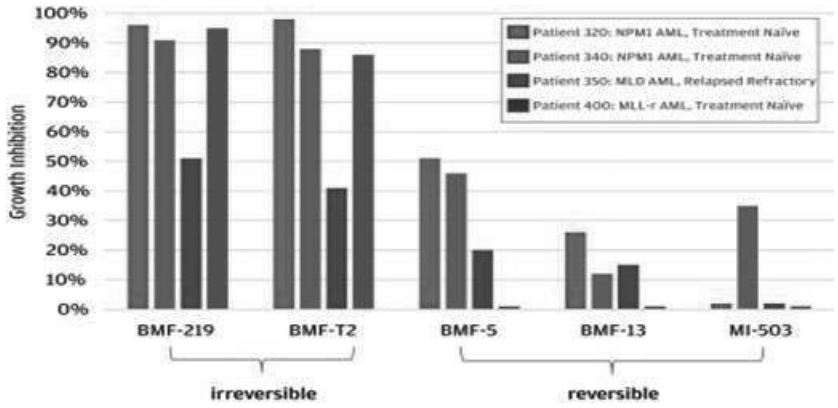
BMF-219 exerted pronounced decrease in menin protein expression in MM and DLBCL cell lines as presented at the IMS Annual Meeting in 2022, "Anti-tumor Activity of Irreversible Menin Inhibitor, BMF-219, in High Grade B-Cell Lymphoma and Multiple Myeloma Preclinical Models" (Poster P-107)

In summary, we have screened the effects of BMF-219 across a range of cancer cell lines and observed potent growth inhibition. These findings support our belief that BMF-219 has significant potential to address a broad range of cancers.

Ex-vivo Studies

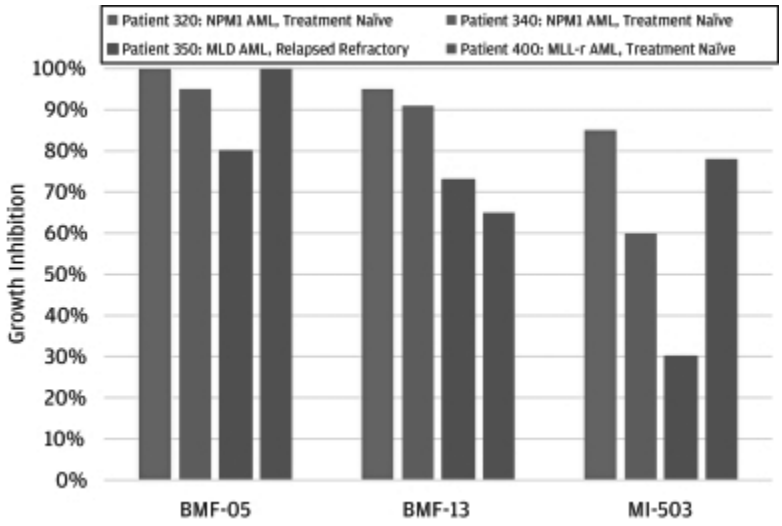
Continuing our focus on the well-characterized menin dependency in leukemia, we investigated patient derived AML samples and the impact of reversible and covalent inhibition of the menin-MLL interaction on proliferation. As reflected in

the figure below, covalent inhibition with BMF-219 and BMF-T2 (a derivative of BMF-219) led to significant growth inhibition and showed substantial advantages over the selected reversible inhibitors.



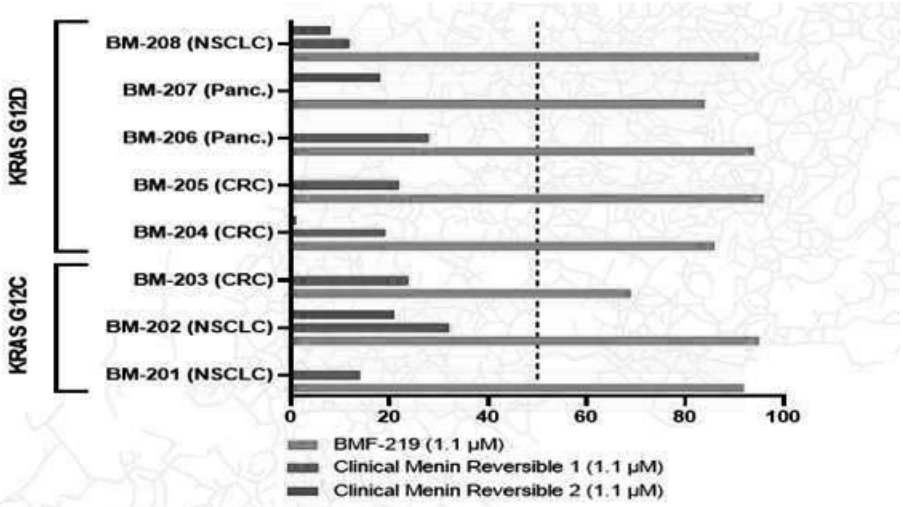
Treatment of patient derived AML cells with menin inhibitors showed potent inhibition of proliferation with covalent drugs (BMF-219 and BMF-T2) versus reversible drugs (BMF-5, BMF-13, MI-503) at 1µM exposure, six days

In comparison, to achieve similar levels of growth inhibition, the selected reversible inhibitors studied required dose concentrations approximately ten-fold greater than our respective IC_{90} values. We believe these findings support our hypothesis that a covalent inhibitor could potentially provide greater therapeutic benefit at lower exposure-levels versus reversible inhibitors.



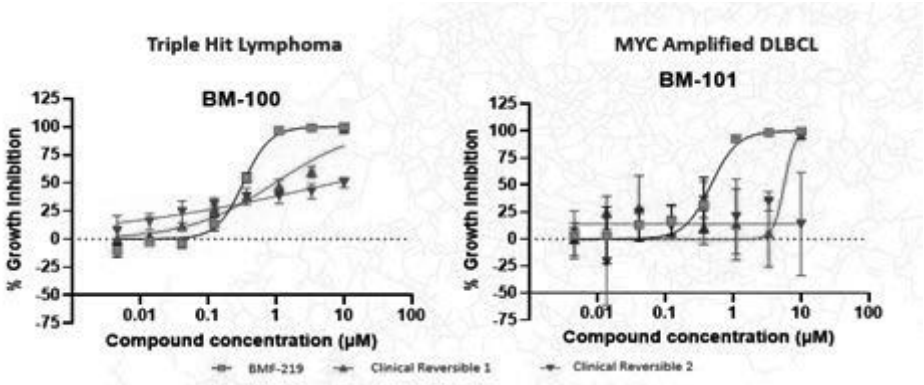
Treatment of patient derived AML cells with reversible menin inhibitors at drug exposures 10-fold greater than IC_{90}(10µM) showed robust inhibition of proliferation at six days

Single agent BMF-219 also produced near complete inhibition of growth at 1.1µM in KRAS G12C and G12D ex-vivo patient samples.



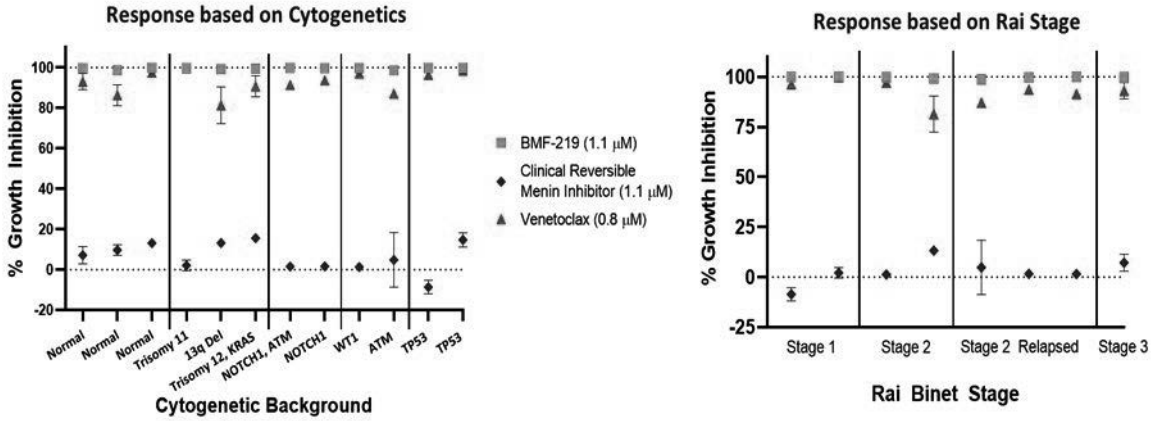
Growth inhibition of ex-vivo KRAS mutant Cells from Patients (1.1 µM Exposure) as presented at the AACR Annual Meeting in 2022, "Irreversible Menin Inhibitor, BMF-219, Exhibits Potent Cytotoxicity in KRAS-Mutated Solid Tumors" (Abstract 2665)

BMF-219 also produced near complete growth inhibition in both THL and MYC amplified DLBCL ex vivo patient samples at approximately1µM exposure. These responses were also superior to clinical reversible (non-covalent) inhibitors with respect to cell growth inhibition at the concentrations tested.



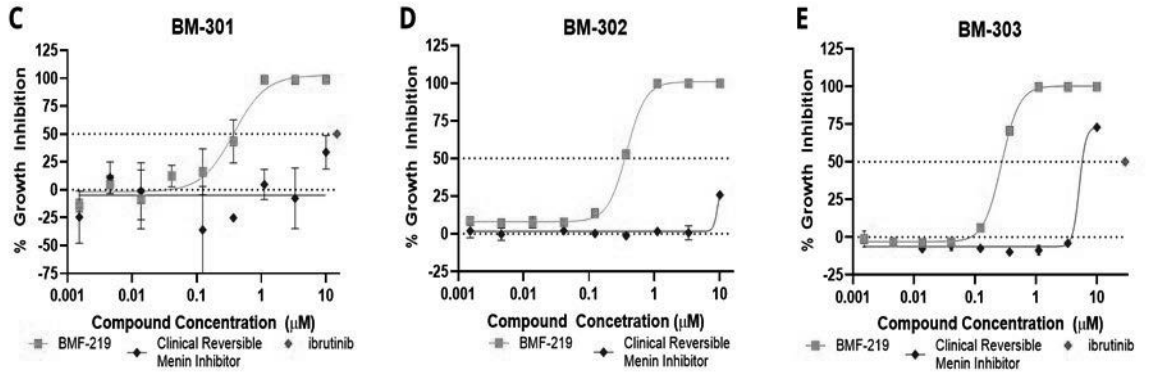
BMF-219 exerted pronounced lethality in DLBCL patient derived models ex vivo as presented at the AACR Annual Meeting in 2022, "Anti-tumor Activity of Irreversible Menin Inhibitor, BMF-219, in High Grade B-Cell Lymphoma and Multiple Myeloma Preclinical Models" (Abstract 2654)

BMF-219 demonstrated broad activity with over 98% cell lethality across *ex vivo* patient-derived CLL tumor models with varying cytogenetic risk profiles and Rai stages, including high- and intermediate-risk cytogenetic profiles which represent a significant unmet clinical need. BMF-219 showed consistently strong activity compared to venetoclax and significantly greater activity than a clinical reversible menin inhibitor. BMF-219 responses were superior to clinical reversible (non-covalent) inhibitors with respect to cell growth inhibition at the concentrations tested.



Growth Inhibition of BMF-219 in patient-derived CLL ex vivo models grouped by genetic background and Rai Stages as presented at the ASCO Annual Meeting in 2022, "Preclinical Activity of irreversible menin inhibitor, BMF-219, in Chronic Lymphocytic Leukemia" (Abstract 7541)

Additionally, BMF-219 exhibited robust growth inhibition in patient samples that were less responsive to standard-of-care agents bendamustine and ibrutinib. Representative dose response curves for BMF-219 or clinical reversible menin inhibitor are shown for patient-derived samples from CLL patients displaying clinical profiles of progression after prior therapy with bendamustine (C) or ibrutinib (D), or ibrutinib pretreated and subsequently progressed on ibrutinib and venetoclax (E).



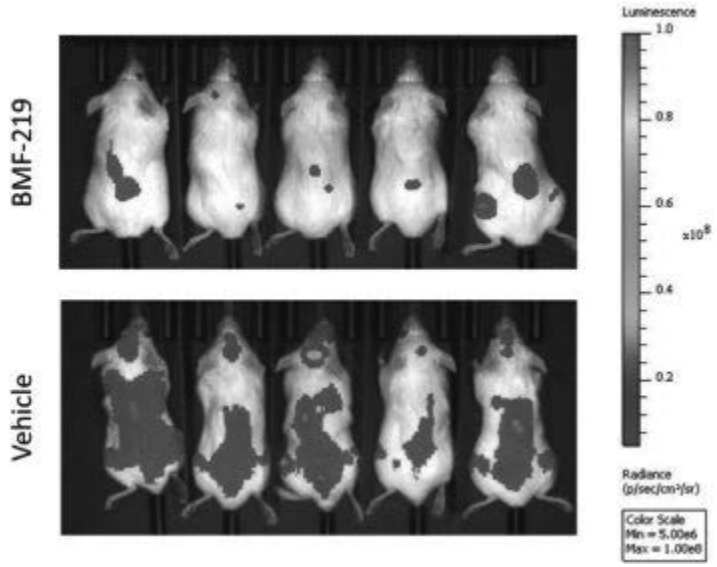
Clinical samples with progression after prior treatment with bendamustine or ibrutinib as presented at the ASCO Annual Meeting in 2022, "Preclinical Activity of irreversible menin inhibitor, BMF-219, in Chronic Lymphocytic Leukemia" (Abstract 7541)

In-vivo Studies

A xenograft model using a MV4;11 leukemia cell line was used to evaluate the potency of BMF-219 as a single agent. We utilized a luciferase transduced MV4;11 model over sub-cutaneous models as we believe the disseminated model better reflects the normal etiology of leukemias, including homing of leukemic cells to the bone marrow and spleen. Also, the disseminated model offered the ability to frequently monitor disease progression through fluorescence imaging which provided a more detailed understanding of the kinetics of the observed response to therapy.

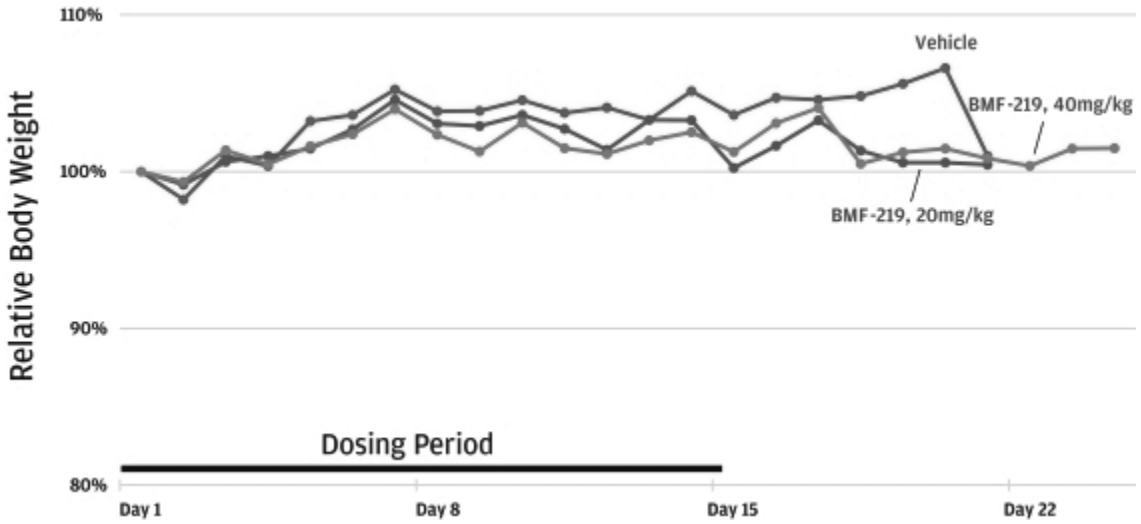
Disseminated MV4;11-luc models were run in female NSG mice. Mice were inoculated with xenograft cancer cells at high levels ($1x10^7$ MV4;11 cells) with greater than 90% viability via tail vein injection. BMF-219 or vehicle was administered (once daily) at various dose levels and via various routes (intravenously (IV), PO: 80-160 mg/kg, IP: 40-80 mg/kg).

As reflected in the figure below, the MV4;11-luc disseminated xenograft study showed substantial tumor reduction and survival benefit for BMF-219 treatment at both the 20 mg/kg and 40 mg/kg doses. Fluorescence imaging showed notable reductions in tumor burden between the control (vehicle treated) animals as compared to the BMF-219 treated animals. Both tested doses showed substantial reductions in tumor burden (-47% at 20 mg/kg; -63% at 40 mg/kg), which translated into survival benefit (over vehicle control) of 72% and 94% for the respective doses (calculated using total days of survival versus control).



Fluorescence imaging of the disseminated MV4;11-luc xenograft model treated for 14 days at 40mg/kg with BMF-219 vs. control. Pseudo-colored area and intensity indicates level of tumor burden

Mean body weight data from our xenograft studies provided an early assessment of safety and tolerability showing that BMF-219 treatment was generally well-tolerated at various doses in a rodent model system. BMF-219 was administered once daily at 20 mg/kg or 40 mg/kg via IV for 14 days and caused minimal changes in body weight from baseline or vehicle control.

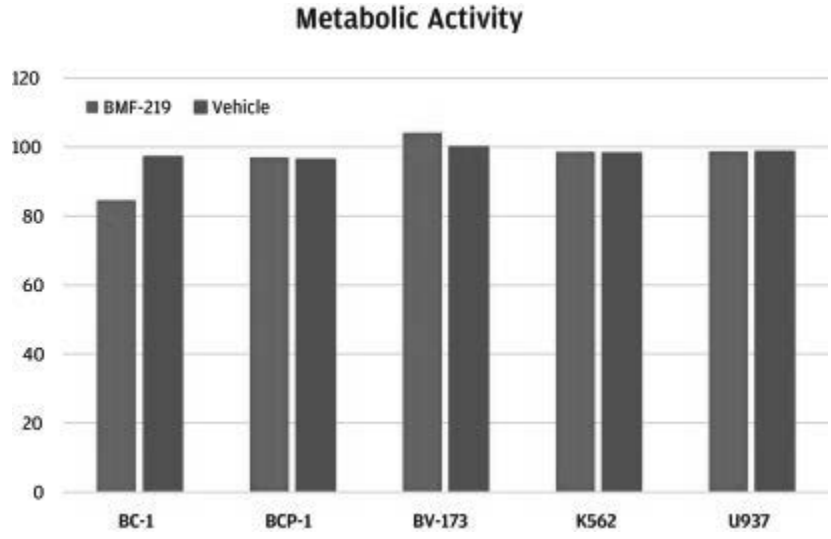


Body weight with BMF-219 treatment showed limited change from baseline and vehicle controls

We have also completed seven-day, non-GLP toxicology studies in rats and dogs where daily oral administration of BMF-219 showed that the compound was generally well-tolerated in both species. Additionally, our pharmacodynamic (PD) studies, which dosed daily up to 14 consecutive days, showed that BMF-219 was generally well-tolerated. We believe these results further support the advancement of BMF-219 into IND-enabling toxicology studies.

OncoPanel Screening

We examined the selectivity of BMF-219 for menin-dependent disease to assess potential off-target risk. We observed negligible impact of BMF-219 treatment on cell metabolism in leukemia and lymphoma cell lines that have wild type MLL, but no menin-linked mechanism for disease. We believe these findings were consistent with external studies showing that menin-MLL interaction was not generally cell-essential and only critical to survival in those cells that contain aberrant biology.



Screening of metabolic activity in BMF-219 treated cells with WT MLL, but no menin-driven disease mechanism showed negligible impact on viability. 0.25μM exposure. The cell lines BC-1, BCP-1, BV-173, K562, and U937 were composed of, respectively, cells that were hematopoietic (B lymphoblast), hematopoietic (B lymphoblast), leukemia (B-cell pre), hematopoietic (bone marrow), and hematopoietic (bone marrow)

Kinase Screening

We have also conducted extensive in-house comparative 3D structural analysis of the protein, which has revealed that the binding pocket we seek to target on menin showed limited structural similarity to some tyrosine kinases known to be of functional relevance in hematological cancers. At a standard compound test concentration of 0.1 µM, BMF-219 displayed high selectivity and limited off-target kinase inhibition. Of the 169 kinases tested, only six showed any inhibition by any of our novel molecules tested. Furthermore, only two wild type kinases showed greater than 50% inhibition upon treatment with BMF-219. We believe this result supports the potential of our FUSION System to generate target-specific compounds.

Glutathione Reactivity

We have also employed the widely used glutathione (GSH) reactivity assay to investigate potential non-specific binding liabilities from electrophilic residues necessary to enable covalent binding. The assay measures the depletion of the tested drug as it forms non-specific complexes with the strong nucleophile GSH and returns drug half-life ($t_{1/2}$) as a readout. Drugs with limited non-specific interactions have long half-lives, as the drug does not get consumed in a reaction with GSH. In such studies, BMF-219 showed negligible interaction with the strong nucleophile GSH and showed less reactivity than the approved covalent drugs omeprazole and neratinib. We believe this result, if replicated in humans, could lead to less non-specific binding and potential off-target effects for BMF-219. The table below shows GSH reactivity studies demonstrating limited non-specific binding liability of BMF compounds. 1µM of compound was incubated with 5 mM of glutathione (5,000 eq).

Drug	Mean half-life (min)
Omeprazole	123.3
Neratinib	197.7
Ibrutinib	>360
BMF-213	322.3
BMF-214	>360
BMF-219	>360

Glutathione reactivity of BMF-219 as compared to other drug and drug candidates

Safety Screen

In order to investigate the safety of BMF-219, we have assayed a selective group of compounds (including BMF-219) at 10 µM on the SafetyScreen 44 panel (CEREP/Eurofins Discovery). This panel was created from the collective experience of multiple large pharmaceutical companies. Our findings showed no meaningful impact (greater than 50% activation or inhibition) of BMF-219 across these key safety assays.

Drug Properties

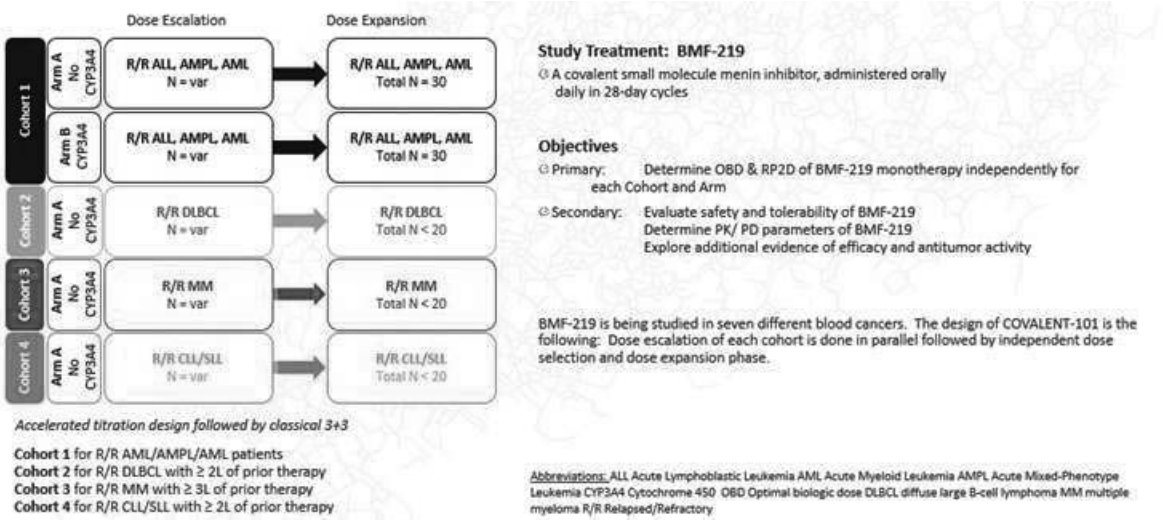
We believe the results observed for BMF-219 in our preclinical studies suggest the potential for this compound to be evaluated as an oral, once-daily treatment for menin driven cancers. With limited formulation work, the compound showed favorable pharmacokinetic (PK) and PD results, and bioavailability that enabled sufficient exposure for us to conduct *in vivo* efficacy and safety studies with oral dosing in mouse, rat, and dog studies. We also tested the metabolic stability of BMF-219 in preclinical studies and have observed no cytochrome (CYP) inhibition to date.

BMF-219 – Clinical Development in Oncology

We are developing BMF-219 for the treatment of liquid and solid tumors that are highly dependent on menin, including leukemias containing the MLL fusion protein. In September 2021, we announced that the U.S. FDA had cleared our IND application to begin a Phase 1 trial of BMF-219 (COVALENT-101) in adult patients with R/R acute leukemia including those with an MLL/KMT2A (Mixed Lineage Leukemia/Lysine Methyl Transferase) gene rearrangement or nucleophosmin 1 (NPM1) mutation. In December 2021, we amended our IND to include subsets of MM and DLBCL patients. In January 2022, we announced the dosing of the first leukemia patient in our COVALENT-101 trial and in June 2022, we announced the dosing of the first patient in the MM cohort of COVALENT-101. In September 2022, we amended the IND to also

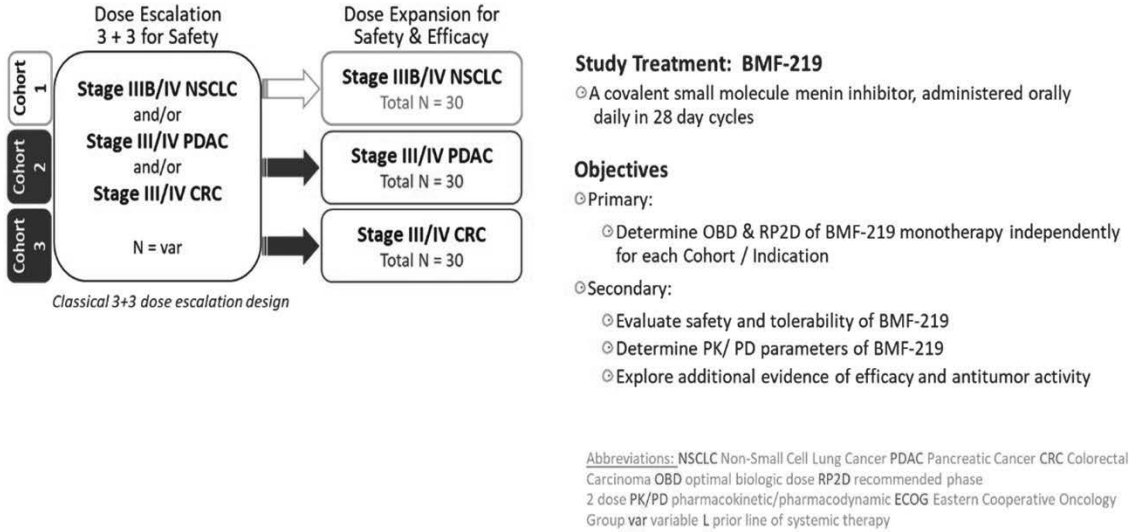
include subsets of patients with chronic lymphocytic leukemia (CLL) and announced the dosing of the first patient in the CLL cohort in October 2022.

COVALENT-101 is an ongoing Phase 1 first-in-human dose-escalation and dose-expansion study of BMF-219 in adult patients with R/R hematologic malignancies (NCT05153330). The study is enrolling four cohorts: AML/ALL (Cohort 1), DLBCL (Cohort 2), MM (Cohort 3) and CLL (Cohort 4).



COVALENT-101 trial design (NCT05153330)

In October 2022, we announced FDA clearance of the IND application for BMF-219 in KRAS mutant solid tumors and the initiation of a Phase 1/1b clinical trial (COVALENT-102). COVALENT-102 is examining BMF-219 as a monotherapy in patients who have unresectable, locally advanced, or metastatic NSCLC, CRC or PDAC with a KRAS mutation. A targeted pan-KRAS inhibitor has the potential to treat the estimated 25-35% of NSCLC, 35-45% of CRC, and approximately 90% of PDAC patients with a KRAS mutation. In January 2023, we announced the dosing of the first patient in the COVALENT-102 study.

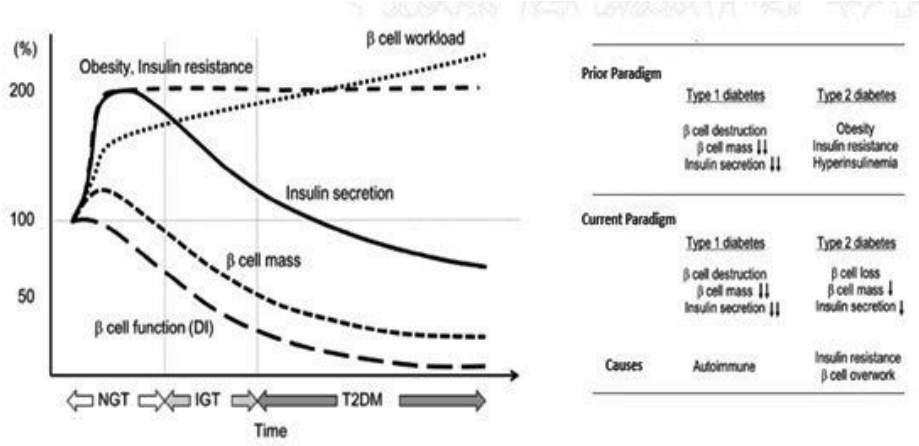


COVALENT-102 trial design (NCT05631574)

BMF-219 – in Diabetes

BMF-219 Tested in Two Diabetes Animal Models

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. Insulin is a hormone that helps the body use glucose for energy and helps control blood glucose levels. In patients with diabetes, beta cell mass and function are diminished, leading to insufficient insulin secretion and hyperglycemia. Insulin resistance leads to an increase in beta cell workload, which ultimately leads to beta cell failure and death and the progression of type 2 diabetes. Type 1 and type 2 diabetes result in beta cell loss and reduction in beta cell mass.



Diabetes progression of type 1 and type 2 driven by beta cell loss

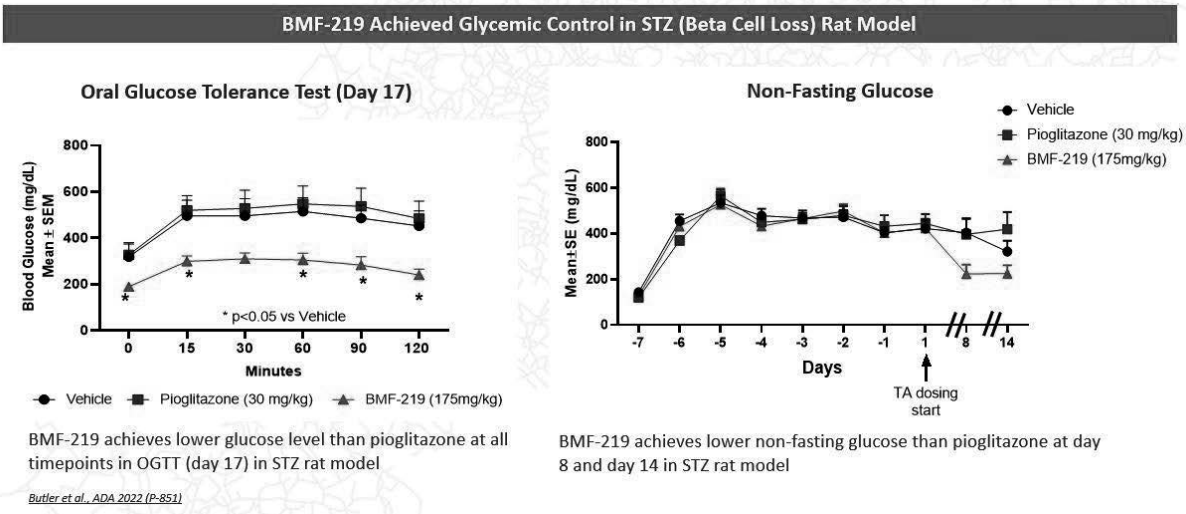
Menin is thought to act as a brake on beta cell turnover / beta cell growth, supporting the notion that inhibition of menin could lead to the regeneration of normal healthy beta cells. Notably, it has previously been shown that knocking out the gene responsible for the creation of menin (*MEN1*) produced profound glycemic control in diabetic animal models. Based on these and other scientific findings, Biomea explored the potential for menin inhibition with BMF-219 as a viable therapeutic approach to permanently halt or reverse progression of type 2 diabetes.

We conducted two diabetes animal experiments to measure the potential impact of BMF-219 for the treatment of type 2 diabetes; the Zucker Diabetic Fatty (ZDF) rat, a widely studied model of obesity and insulin resistance in rats, and the Streptozotocin-Induced Diabetes (STZ) induced rat, a widely studied model by which diabetes is induced using an antibiotic (STZ) that produces pancreatic islet β-cell destruction. In both models, we observed that BMF-219 worked to normalize glucose levels in the majority of animals after just two weeks of treatment. Notably, the majority of the effect was maintained despite complete washout of BMF-219 in ZDF rats.

Two diabetes preclinical models interrogating the therapeutic effect of BMF-219

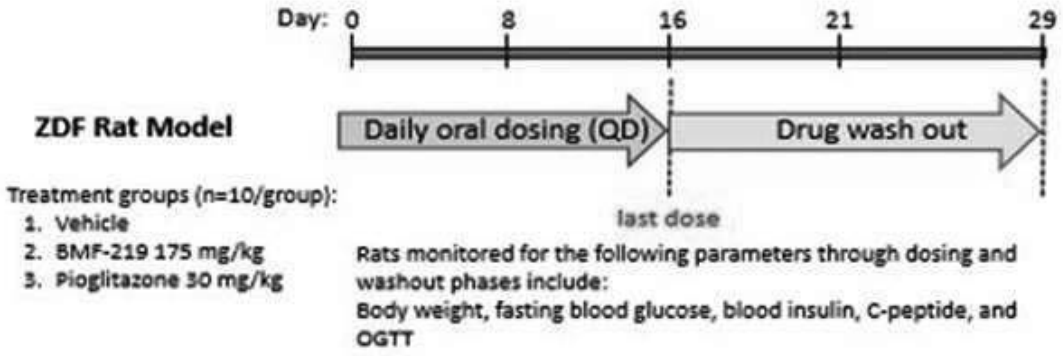
We presented data from these experiments at the 2022 ADA Annual Meeting Scientific Sessions, which showed BMF-219's strong, prolonged glycemic control, insulin sensitization, and HbA1c reduction in two preclinical rat models of diabetes. At the ADA, we featured results from preclinical studies testing BMF-219 in two separate Zucker Diabetic Fatty (ZDF) rat models against pioglitazone (a thiazolidinedione) and liraglutide (a Glucagon like Peptide-1 agonist) and also against

pioglitazone in a streptozotocin (STZ)-induced rat model. Notably, BMF-219 was superior to pioglitazone in an oral glucose tolerance test (OGTT), an assessment of glucose metabolism and processing, in the STZ beta cell ablation model during the treatment period. In this model, BMF-219, but not the active comparator, pioglitazone, restored non-fasting glucose levels to near normal baseline by treatment day eight and significantly reduced blood glucose levels compared to vehicle and pioglitazone during an OGTT in STZ rats (mean AUC reduction of 41%, $p<0.05$) at day 17, suggesting that BMF-219 rapidly induced pancreatic beta cell regrowth and function.

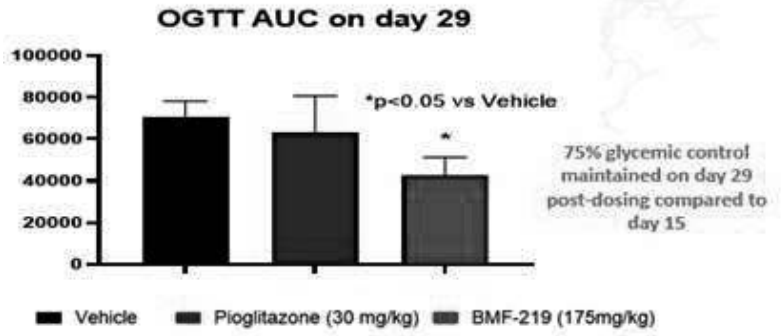


BMF-219 demonstrated strong activity in beta cell loss animal model (STZ Rat) as presented at the ADA Annual Meeting in 2022, "Oral Long-Acting Menin Inhibitor Normalizes Type 2 Diabetes Mellitus (T2DM) in Two Rat Models"

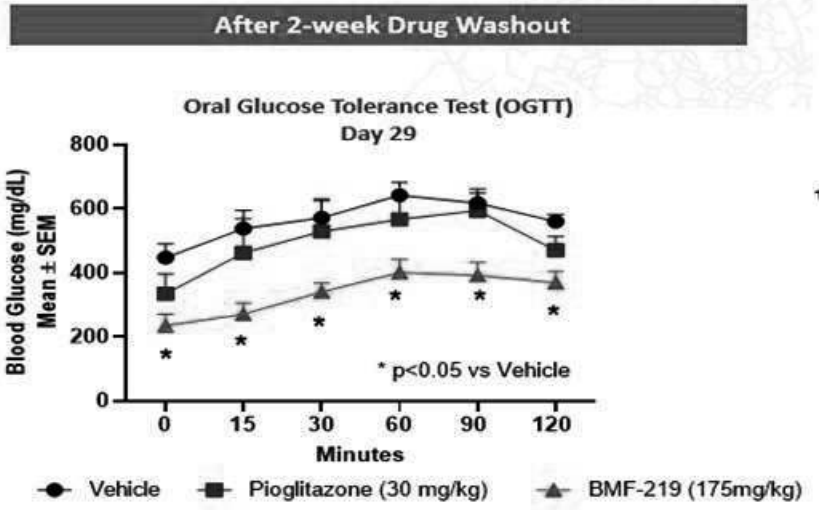
BMF-219 also achieved glycemic control via similar assessments in both ZDF models at all timepoints, including superior glycemic control compared to pioglitazone after the washout period. In the ZDF model, BMF-219 and pioglitazone showed similar glycemic control during an OGTT while the drug was present (AUC reduction of 54%, $p<0.001$) but only BMF-219 treated rats saw weight loss while on the drug and maintained glycemic control two weeks after washout (AUC reduction of 40%, $p<0.05$), which indicated prolonged glycemic control.



ZDF rat preclinical trial experiment. Rats treated with BMF-219, pioglitazone or vehicle control for 16 days were monitored for blood glucose levels by OGTT on day 29, ~2 weeks after administration of the last dose, as presented at the ADA Annual Meeting in 2022, "Oral Long-Acting Menin Inhibitor Normalizes Type 2 Diabetes Mellitus (T2DM) in Two Rat Models"

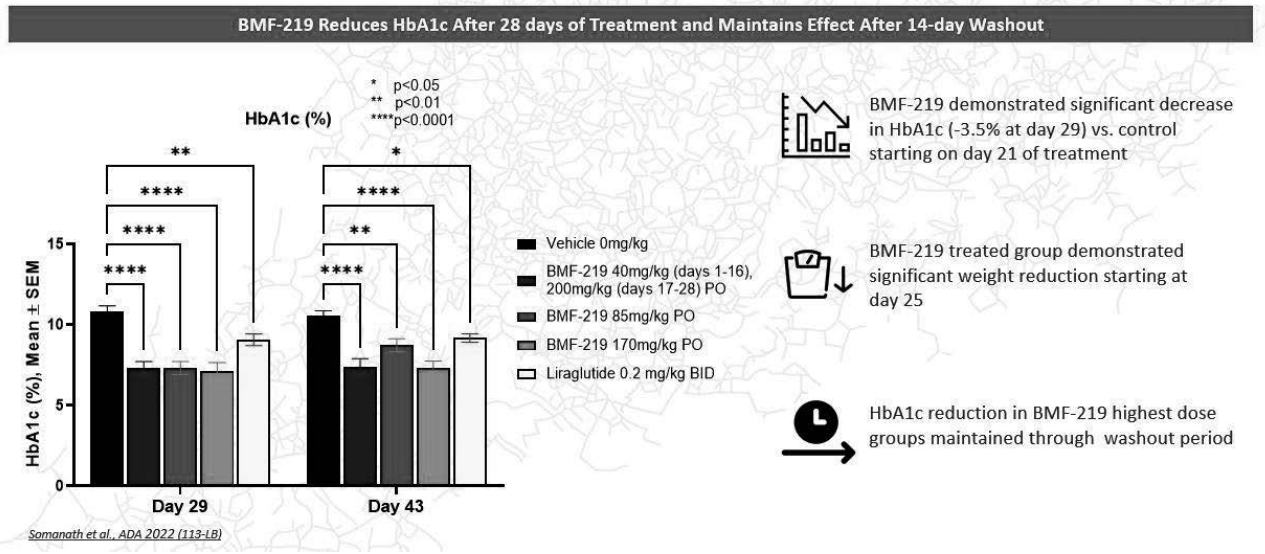


ZDF rats treated with BMF-219 showed ~2 weeks after administration of the last dose an AUC reduction of 40%, (p<0.05) as presented at the ADA Annual Meeting in 2022, "Oral Long-Acting Menin Inhibitor Normalizes Type 2 Diabetes Mellitus (T2DM) in Two Rat Models"



BMF-219 displayed durable glycemic control during drug washout and two weeks after the last dose as presented at the ADA Annual Meeting in 2022, "Oral Long-Acting Menin Inhibitor Normalizes Type 2 Diabetes Mellitus (T2DM) in Two Rat Models"

A four-week BMF-219 treatment in ZDF rats also resulted in a significant reduction in HbA1C at Day 21, which reached 3.5% absolute reduction versus vehicle, compared to liraglutide (1.7% at Day 29), and remained reduced throughout the entire study, including post-treatment. At all BMF-219 doses, this significant reduction in HbA1C in ZDF rats was maintained during the 15-day washout period after the last dose and significant reduction in HbA1c was maintained after drug washout by only BMF-219, while the lowering of HbA1c by liraglutide vs. control on Day 43 was not statistically significant. In addition to OGTT, blood glucose, insulin, C-peptide, HbA1c lipemic levels, and weight were also assessed.



BMF-219 demonstrated strong activity in insulin resistant animal model (ZDF Rat) as presented at the ADA Annual Meeting in 2022, "BMF-219, displays a significant and durable reduction in HbA1c in a Type 2 Diabetes Mellitus Rat Model"

In September 2022, we presented additional data in two oral abstracts ("Oral Menin Inhibitor, BMF-219, displays a significant and durable reduction in HbA1c in a Type 2 Diabetes Rat Model" and "Oral Long-Acting Menin Inhibitor, BMF-219, Normalizes Type 2 Diabetes Mellitus in Two Rat Models") at the European Association for the Study of Diabetes (EASD) Annual Meeting in Stockholm, Sweden. Treatment with BMF-219 led to an increase in beta cell mass in *ex vivo* experiments with human donor islets and displayed the ability to restore and preserve beta cell function in two animal models of type 2 diabetes. BMF-219 showed improved pancreatic beta cell function and beta cell area, insulin sensitivity, blood lipid levels, weight decline, and glycemic control in the rat models (ZDF and the STZ) during the dosing period, and importantly, glycemic control was maintained after the dosing period ended. BMF-219 treatment resulted in a sustained increase in beta cell area and function in the ZDF diabetic rats observed at the end of treatment and two weeks following succession of therapy, compared to rats treated with vehicle or active control pioglitazone, which showed a decline in beta cell area and function.

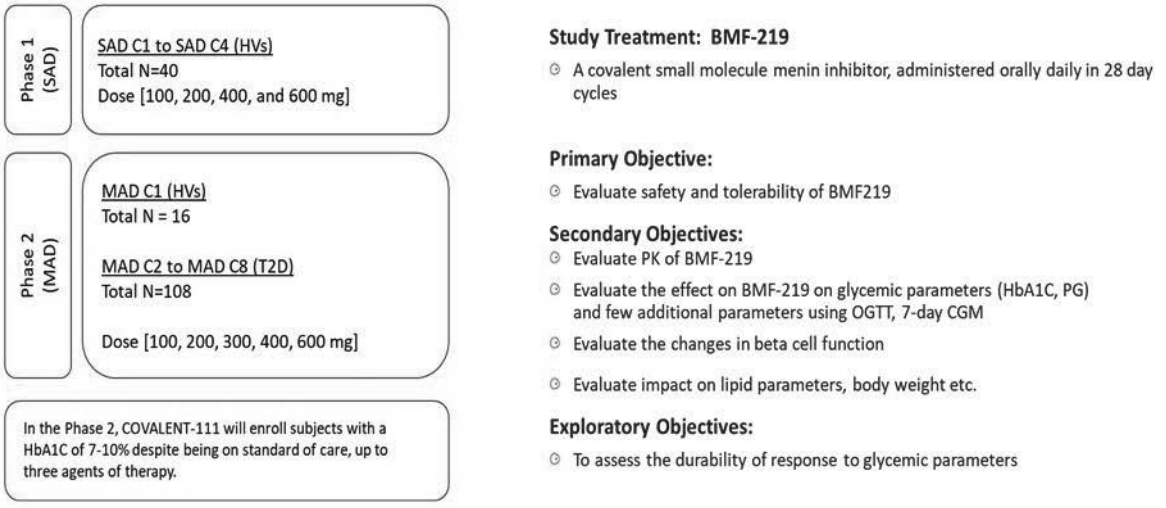
We believe BMF-219 is an innovative, investigational molecule with paradigm shifting potential for the treatment of diabetes. BMF-219 is being developed as an oral and transient treatment for the regeneration, preservation, and reactivation of beta cells with a durable effect after drug discontinuation. BMF-219 may be disease modifying via the restoration of beta cell homeostasis. BMF-219 may also be synergistic with GLP-1 based treatments while potentially insulin sparing. A potential utility for BMF-219 may be in the prevention of type 2 diabetes (as there are over 90 million prediabetic patients in the U.S.). The use of BMF-219 may also lead to the potential reduction in insulin dependence. We also believe BMF-219's mechanism of action and impact on beta cells may have a positive impact even on other related diseases, including nonalcoholic steatohepatitis (NASH), chronic kidney disease **(**CKD) and cardiovascular disease (CV).

BMF-219 – Clinical Development in Diabetes

In October 2022, we announced the completion of the Phase 1 portion of COVALENT-111 in healthy volunteers in Canada and the dosing of the first patient with type 2 diabetes in the Phase 2 portion of COVALENT-111, also in Canada. In the completed Phase 1 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. BMF-219 was well tolerated and showed a favorable PK and PD profile.

In December 2022, we announced the clearance of the IND by the FDA for BMF-219 in type 2 diabetes to support the expansion of COVALENT-111 to sites in the U.S. The ongoing Phase 2 portion consists of multiple ascending dose cohorts and includes adult patients with type 2 diabetes uncontrolled by current therapies. It is designed to examine the capacity of BMF-219 to enable the proliferation, preservation, and reactivation of healthy, functional beta cells capable of producing

insulin, thereby leading to long-term glycemic control. In January 2023, we announced the dosing of the first patient with type 2 diabetes in the United States.



COVALENT-111 trial design (NCT05731544)

On March 28, 2023, we reported topline initial clinical data from the Phase 2 portion of COVALENT-111. 40 subjects were enrolled in the first three cohorts of COVALENT-111, with the first cohort comprising 16 healthy volunteers (HVs) exposed to 100 mg BMF-219 once daily for two weeks. In Cohorts 2 and 3, subjects with type 2 diabetes (T2DM) (n=12 per cohort with 10 subjects treated with BMF-219 and 2 subjects on placebo) received BMF-219 once daily for four weeks with or without food, respectively. In the two diabetes cohorts, enrolled patients had T2DM diagnosed for ≤15 years, were ages 18 to 65, had a BMI ≥25 and ≤40 kg/m^2, and had uncontrolled diabetes with HbA1c ≥7.0% and ≤10% despite being on up to three standard-of-care diabetes therapies. At baseline, patients enrolled in Cohorts 2 and 3 had a median A1c of 7.9% and 7.8%, respectively.

Active treatment Cohort 3 (BMF-219 without food) compared to Cohort 2 (BMF-219 with food) showed a positive dose-response pharmacokinetics relationship demonstrated by about a threefold median increase in C_{max} (ng/ml) and AUC (ng x h/ml) when BMF-219 was administered without food. This increase in BMF-219 systemic exposure was in line with the differences seen in the response rates between the two cohorts. Specifically, the change in HbA1c at four weeks for Cohort 3 patients (n=9) on BMF-219 (100 mg, without food) showed a median A1c reduction of -1.0% and a 89% (8/9) response rate at four weeks, with 78% of subjects achieving a ≥0.5% reduction in A1c and 56% achieving a ≥1.0% reduction in A1c. Cohort 2 patients (n=10) on BMF-219 (100 mg, with food) showed a median A1c reduction of -0.3% and a 70% (7/10) response rate at four weeks, with 30% of subjects achieving a ≥0.5% to ≤1.0% reduction in A1c. Placebo patients (n=4) showed a median and mean A1c reduction between -0.1% and -0.15%.

We also reported on the tolerability profile of BMF-219 observed in Cohorts 1, 2, and 3 of COVALENT-111. During the HV portion of the study, in Cohort 1 (n=16), we observed minor Grade 1 Treatment Emergent Adverse Events (TEAEs) and no TEAEs were considered related to BMF-219. During the dosing of diabetes patients in Cohorts 2 and 3 all TEAEs observed were Grade 1, except for an asymptomatic laboratory finding of Grade 2 elevated lipase in a single subject that was considered unrelated to BMF-219. In summary, BMF-219 was generally well-tolerated.

Other Clinical and Preclinical Programs

Beyond BMF-219, we are utilizing our novel platform to develop covalent treatments against other high-value oncogenic drivers of cancer. In May 2022, we announced our second development candidate, BMF-500, a covalent inhibitor of FLT3. BMF-500 is being developed as a highly potent and selective, covalent, small molecule inhibitor of FLT3, that is designed to bind irreversibly to a reactive cysteine in the kinase active site.

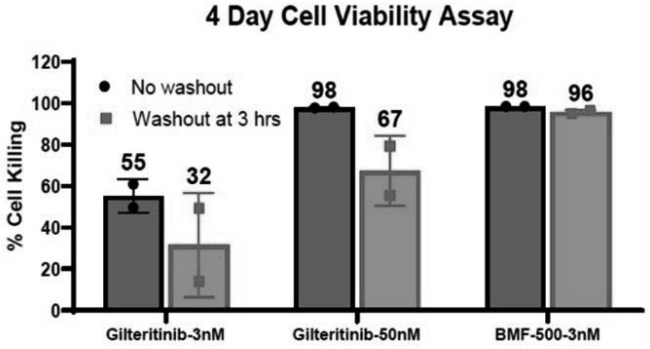
BMF-500 is a third-generation covalent inhibitor of FLT3, which, in preclinical studies has demonstrated picomolar IC_{50} values across key FLT3 isoforms, potentially making it the most potent inhibitor of its class. Activating mutations of the FMS-like tyrosine kinase 3 (FLT3) are the most frequent genetic alteration in AML and are associated with poor prognosis. Though several FLT3 inhibitors have entered clinical trials and reached commercialization, adverse events and dose-limiting

toxicities often restrict the therapeutic window and limit their long-term use. Such limitations can impact the ability to achieve long-lasting response in patients and ultimately result in therapy-induced resistance.

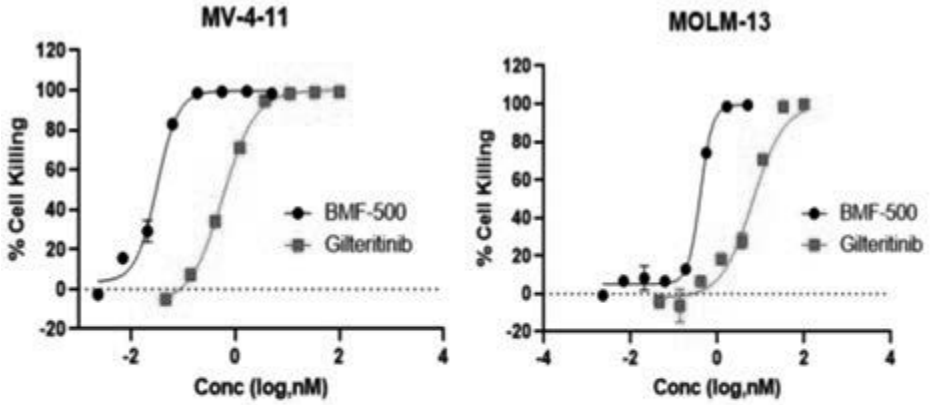
At the ASH Annual Meeting in December 2022, we presented preclinical data supporting the potential of BMF-500 as a highly potent and selective FLT3 inhibitor. The presentation described BMF-500's picomolar affinity to activating FLT3 mutations including FLT3 internal tandem duplications (FLT3-ITD) and various tyrosine kinase domain (TKD) mutations, multi-fold higher potency and increased cytotoxicity than commercially available non-covalent FLT3 inhibitor gilteritinib, and complete tumor regression at physiologically relevant doses in mouse models of FLT3-ITD AML and maintenance of effect without continued exposure. BMF-500 selectively killed AML cells harboring FLT3 activating mutations, including MV4-11 and MOLM-13, and engineered cells expressing FLT3-ITD and/or FLT3 TKD mutations. In *ex vivo* cultures, BMF-500 as a single agent induced potent growth inhibition of patient-derived AML cells harboring either FLT3-ITD or FLT3 non-ITD mutations.

The potent covalent inhibition of FLT3 by BMF-500 manifested durable cellular response that was improved over gilteritinib. A three-hour exposure followed by wash-out of BMF-500 outperformed four days of continuous exposure to gilteritinib, at all concentrations tested. In cells harboring FLT3 activating mutations, BMF-500 induced dose-dependent inhibition of FLT3 phosphorylation and downstream signaling, including phospho-STAT5 and phospho-ERK. A 1-hour pulse treatment with BMF-500 was sufficient to achieve deep and durable target inhibition for greater than 24 hours, an effect not observed with gilteritinib under similar conditions.

Potent FLT3 inhibition and high selectivity of BMF-500 translated to sustained tumor regression and improved survival in both subcutaneous and disseminated xenograft models of mutant FLT3-driven AML. Orally administered BMF-500 was well tolerated over four weeks of dosing. We believe BMF-500 is a novel FLT3 inhibitor, given its activity, durability, and selectivity in comparison to existing FLT3 inhibitors.



Potent and durable target inhibition leading to active cell killing in comparison to gilteritinib as presented at the ASH Annual Meeting in 2022, "BMF-500: An Orally Bioavailable Covalent Inhibitor of FLT3 with High Selectivity and Potent Antileukemic Activity in FLT3-Mutated AML" (Abstract 2756)



Compound ID	MV-4-11 IC_{50} (nM)	MOLM-13 IC_{50} (nM)
BMF-500	0.03	0.30
Gilteritinib	1.7	6.5

Potent Cell-Based Activity in AML Cell Lines with FLT3 Mutations as presented at the ASH Annual Meeting in 2022, "BMF-500: An Orally Bioavailable Covalent Inhibitor of FLT3 with High Selectivity and Potent Antileukemic Activity in FLT3-Mutated AML" (Abstract 2756)

NanoBRET Target Engagement Assay, IC_{50} (nM)

Cmpd ID	FLT3 WT	FLT3 (D835H)	FLT3 (D835V)	FLT3 (D835Y)
BMF-500	0.31	0.18	0.22	0.25
Gilteritinib	23.4	1.45	1.1	1.4

FLT3 Inhibitor Resistance Mutations Coverage, IC_{50} (nM)

Cmpd ID	FLT3-ITD	FLT3-ITD-D835Y	FLT3-ITD-F691L
BMF-500	2 nM	5 nM	7 nM
Gilteritinib	7 nM	19 nM	98 nM

Potent coverage of FLT3 inhibitor resistant mutation as presented at the ASH Annual Meeting in 2022, "BMF-500: An Orally Bioavailable Covalent Inhibitor of FLT3 with High Selectivity and Potent Antileukemic Activity in FLT3-Mutated AML" (Abstract 2756)

Competition

The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, intense competition and a strong emphasis on intellectual property. We believe that our approach, strategy, scientific capabilities, know-how and experience provide us with competitive advantages. In addition, we believe we are currently the only company in the United States developing irreversible covalent binders specifically against menin. More broadly, we define ourselves as targeted oncology drug developers focused on irreversible covalent drugs and as such expect substantial competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions and governmental agencies and public and private research institutions worldwide. Many of our competitors, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also

prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies may be or may become interested in discovery and development of irreversible covalent binders that may compete with us against menin or related targets at scale and in an integrated way. Even if they do not advance programs with the same mechanism of action as ours, these companies could develop products or product candidates that are competitive with ours or that have a superior product profile, and may do so at a rapid pace. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do. We face competition from segments of the pharmaceutical, biotechnology and other related markets that pursue the development of therapies that target irreversible covalent binding against protein targets of interest to us.

To our knowledge, there are several programs that target menin in clinical development for acute leukemias at this time; we are aware of Kura Oncology's KO-539 and Syndax Pharmaceuticals' SNDX-5613, both of which target the menin-MLL1 interaction through the use of non-covalent inhibition. Both KO-539 and SNDX-5613 are in clinical development and have demonstrated Phase 1 results that support continued development into pivotal studies and validate menin as a therapeutic target. Other clinical programs have been reported by Daiichi Sankyo (DS-1594), Janssen Pharmaceuticals (JNJ-75276617) and Sumitomo Pharma Oncology (DSP-5336). Additionally, other preclinical programs have been reported by Bayer (BAY-155), Novartis, and the University of Michigan.

Our competitors will also include companies that are or will be developing other targeted therapies, including small molecule, antibody, or protein degraders for the same indications that we are targeting. We could see a reduction or elimination in our commercial opportunity if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with more favorable labeling than our product candidates. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their potency, selectivity, inactivation of the target, therapeutic window, safety, convenience, price, the level of generic competition, our ability to market and commercialize the product candidate, and the availability of reimbursement from government and other third-party payors.

Intellectual Property

We seek to protect the intellectual property and proprietary technology that we consider important to our business, including by pursuing patent applications that cover our product candidates and methods of using the same, as well as other relevant inventions and improvements that we believe to be commercially important to the development of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. Our commercial success depends, in part, on our ability to obtain, maintain, enforce and protect our intellectual property and other proprietary rights for the technology, inventions and improvements we consider important to our business, and to defend any patents we may own or in-license in the future, prevent others from infringing any patents we may own or in-license in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties. As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending provisional and Patent Cooperation Treaty (PCT) applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents and any issued patents we may obtain do not guarantee us the right to practice our technology or commercialize our product candidates. The PCT is a treaty with more than 150 contracting states that makes it possible to seek patent protection across multiple states by filing a single "international" application. We also cannot predict the breadth of claims that may be allowed or enforced in any patents we may own or in-license in the future. Any issued patents that we may own or in-license in the future may be challenged, invalidated, circumvented or have the scope of their claims narrowed. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide.

The term of individual patents depends upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office (USPTO) in examining and granting a patent, or may be shortened if a patent is terminally disclaimed

over an earlier filed patent. The term of a patent claiming a new drug product may also be eligible for a limited patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The extension period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of a new drug application, plus the time between the submission date of a new drug application and the ultimate approval date. The extension period cannot be longer than five years and the total patent term, including the extension period, must not exceed 14 years following FDA approval. Only one patent applicable to an approved product is eligible for the extension, and only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended. A patent that covers multiple products for which extension is sought can only be extended in connection with one of the approvals. The USPTO reviews the application for any patent term extension or restoration in consultation with the FDA. In the future, if any of our product candidates receive approval by the FDA, we expect to apply for a patent term extension on an issued patents covering the product, depending upon the length of the clinical studies for the product and other factors. Outside the U.S., similar applications for patent term extensions or supplementary protection certificates are available in a limited number of countries. We expect to apply for such coverage where available. There can be no assurance that the USPTO or any other patent office outside the U.S. will approve any of our applications for patent term extensions or supplementary protection certificates. There can be no assurance that patents will issue from our current or future pending patent applications, or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future. In addition, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Patent term may be inadequate to protect our competitive position on our products, if approved, for an adequate amount of time.

As of December 31, 2022, we owned two issued U.S. patents, more than fifty U.S. and outside U.S. pending patent applications, directed to compositions of matter, methods of treatment, and methods of making with respect to our product candidates, including BMF-219 and BMF-500.

Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the USPTO or other foreign jurisdiction are often significantly narrowed by the time they issue, if they issue at all. Any of our pending PCT patent applications are not eligible to become issued patents until, among other things, we file national stage patent applications within 30 months in the countries in which we seek patent protection. If we do not timely file any national stage patent applications, we may lose our priority date with respect to our PCT patent applications and any patent protection on the inventions disclosed in such PCT patent applications. Our provisional patent applications may never result in issued patents and are not eligible to become issued patents until, among other things, we file a non-provisional and/or PCT patent application within 12 months of filing the related provisional patent application. If we do not timely file non-provisional or PCT patent applications, we may lose our priority date with respect to our provisional patent applications and any patent protection on the inventions disclosed in our provisional patent applications. While we intend to timely file non-provisional and PCT patent applications relating to our provisional patent applications, and we intend to timely file national stage patent applications relating to our PCT patent applications, we cannot predict whether any of our current or future patent applications related to BMF-219, or any of our other product candidates, will issue as patents. If we do not successfully obtain patent protection, or, even if we do obtain patent protection, if the scope of the patent protection we obtain our product candidates or technology is not sufficiently broad, we will be unable to prevent others from using our technology or from developing or commercializing technology and products similar or identical to ours or other competing products and technologies. Additionally, even if any of our patent applications issue as patents, the patents covering our proprietary technologies and our product candidates would be expected to expire between 2039 to 2042.

In addition to patent applications, we rely on unpatented trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential know-how are difficult to protect. In particular, we consider various aspects of our irreversible binder discovery platform to constitute our trade secrets and know-how. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors and non-competition, non-solicitation, confidentiality and invention assignment agreements with our employees and consultants. We cannot guarantee that we will have executed such agreements with all applicable employees and contractors, or that these agreements will afford us adequate protection of our intellectual property and proprietary information rights. In addition, our trade secrets and/or confidential know-how may become known or be independently developed by a third party or misused by any person to whom we disclose such information. These agreements may also be breached, and we may not have an adequate remedy for any such breach. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. Although we take steps to protect our product candidates or any future proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information.

For more information regarding the risks related to our intellectual property, please see "Risk Factors—Risks related to our intellectual property."

License and Partnership Agreements

As of December 31, 2022, we do not have any license or partnership agreements related to any of our programs. As these programs and our business evolves we may consider entering into a potential license or partnership. A potential partnership could provide non-dilutive funding and access to additional capabilities and expertise that a partner could provide to enhance the overall probability of program success.

Manufacturing

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates undergoing preclinical studies, as well as for our clinical trials. This arrangement is also expected for commercial manufacturing if our product candidates receive marketing approval. Certain of our suppliers of ingredients, raw materials, components and materials are single source suppliers. All of our product candidates are small molecules and are manufactured in synthetic processes from available starting materials. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Commercialization

Subject to receiving marketing approvals, we expect to commence commercialization activities by building a focused sales and marketing organization in the United States to sell our products. We believe that such an organization will be able to address the community of oncologists who are the key specialists in treating the patient populations for which our product candidates are being developed. Outside the United States, we expect to enter into distribution and other marketing arrangements with third parties for any of our product candidates that obtain marketing approval. We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, and export and import of drug products. A new drug must be approved by the FDA through the New Drug Application (NDA) process before it may be legally marketed in the United States. We, along with any third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our products and product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory studies, animal studies and formulation studies in accordance with the FDA's good laboratory practice (GLP) requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board (IRB), or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices (GCPs), to establish the safety and efficacy of the proposed drug for its intended use;
- preparation of and submission to the FDA of an NDA after completion of all pivotal trials;

- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the drug is produced to assess compliance with current good manufacturing practice (cGMP) requirements to ensure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, a sponsor must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk.

Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies, may be conducted after initial marketing

approval, and may be used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

In March 2022, the FDA released a final guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how drug developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology drug development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by the FDA. Expansion cohort trials can potentially bring efficiency to drug development and reduce developmental costs and time.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

In addition, during the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

U.S. Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by independent investigators. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the filing date to complete a standard review of an NDA for a drug that is a new molecular entity. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates an NDA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the NDA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the NDA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a risk evaluation and mitigation strategy (REMS) to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use (ETASU), such as restricted distribution methods, patient registries, and other risk minimization tools. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if required. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

In addition, the Pediatric Research Equity Act (PREA) requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, fails to keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the Fast Track program is intended to expedite or facilitate the process for reviewing new products that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a Fast Track product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. A Fast Track product may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically

significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product candidate is eligible for priority review if it is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For new-molecular-entity NDAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period.

Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval do not change the standards for approval, but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population of 200,000 or more individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or in instances of drug supply issues. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other potential benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-approval Requirements

Drug products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic

reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors and those supplying products, ingredients, and components are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Other United States Regulatory Matters

Manufacturing, sales, promotion and other activities of product candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, which may include the Centers for Medicare & Medicaid Services (CMS), other divisions of the Department of Health and Human Services (HHS), the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety

Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

United States Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of our future product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit restoration of the patent term of up to five years as compensation for patent term lost during the FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Regulatory exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated NDA (ANDA), or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides three years of exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent for other conditions of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

In addition, drugs can also obtain pediatric exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

Other Healthcare Laws

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs;
- federal civil and criminal false claims laws, including the False Claims Act (FCA), which can be enforced through civil "qui tam" or "whistleblower" actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other federal health care programs that are false or fraudulent; knowingly making or

causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;

- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating these statutes without actual knowledge of the statutes or specific intent to violate them in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), imposes requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. Even when HIPAA does not apply, according to the Federal Trade Commission (FTC), failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, 15 U.S.C. § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards;

- the federal Physician Payment Sunshine Act, created under the ACA and its implementing regulations, which requires manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations extended to include payments and transfers of value made to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse midwives during the previous year;

- California's California Consumer Privacy Act (CCPA), which went into effect on January 1, 2020, which affords consumers expanded privacy protections. For example, the CCPA gives California residents expanded rights to access and require deletion of their personal information, opt-out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA also provides for civil penalties for violations, as well as a private right of action for data breaches that may increase our risk to data breach class action litigation. The CCPA was expanded substantially on January 1, 2023, when the California Privacy Rights Act of 2020 (CPRA) became fully operative. The CPRA, among other things, gives California residents the ability to limit use of certain sensitive personal information, further restrict the use of cross-contextual advertising, establish restrictions on the retention of personal information, expand the types of data breaches subject to the CCPA's private right of action, provide for increased penalties for CPRA violations concerning California residents under the age of 16, and establish a new California Privacy Protection Agency to implement and enforce the new law;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales, and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives.

Coverage and Reimbursement

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services.

Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Healthcare Reform

In March 2010, the ACA was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, the ACA:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price;

- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administrations or other efforts, if any, to challenge repeal or replace the ACA, will impact our business.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates.

Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. This deadline was pushed back to January 1, 2027 by the Bipartisan Safer Communities Act. The Inflation Reduction Act of 2022 (IRA) further delayed implementation of this rule to January 1, 2032. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

In addition, other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- On August 2, 2011, the U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect until 2032, with the exception of a temporary suspension that

lasted from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the suspension, a 1% payment reduction began April 1, 2022, and remained through June 30, 2022. The 2% payment reduction resumed on July 1, 2022.

- On January 2, 2013, the U.S. American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.
- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.
- On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.
- The IRA was signed into law in August 2022. The IRA includes several provisions that will impact our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. The effect of IRA on our business and the healthcare industry in general is not yet known.

Individual states have also been increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. We expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration, any of which could limit the amounts that federal and state governments will pay for healthcare products and services.

Human Capital Resources

As of December 31, 2022, we had 83 full-time employees, 59 of whom were engaged in research and development activities. We believe we have good relationships with our employees. None of our employees are represented by a labor union or covered under a collective bargaining agreement.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Corporate Information

Biomea Fusion, Inc., (the "Company"), was established in the state of Delaware in August 2017 as Biomea Fusion, LLC. In December 2020, all outstanding membership interests in Biomea Fusion, LLC were converted into equity interests in the Company.

Our principal executive offices are located at 900 Middlefield Road, 4th Floor, Redwood City, California 94063, and our telephone number is (650) 980-9099. Our website address is www.biomeafusion.com. We do not incorporate the information on or accessible through our website into this Annual Report on Form 10-K, and you should not consider any information on, or that can be accessed through, our website a part of this Annual Report on Form 10-K.

Biomea Fusion, Inc., the Biomea logo, FUSION System and our other registered or common law trademarks, trade names or service marks appearing in this Annual Report on Form 10-K are owned by us. This Annual Report on Form 10-K contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K, including logos, artwork and other visual displays, generally appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy and information statements and amendments to reports filed pursuant to Sections 13(a), and 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act) are filed with the U.S. Securities and Exchange Commission (SEC). We are subject to the informational requirements of the Exchange Act and file or furnish reports, proxy statements and other information with the SEC. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at www.sec.gov. Such documents and other information filed by us with the SEC are available free of charge on the "Investors & Media" section of our website when such reports are available on the SEC's website. The contents of websites referred to above are not incorporated into this Annual Report on Form 10-K. Further, our references to the URLs for these websites are intended to be inactive textual references only.

Item 1A. Risk Factors

Our business is subject to various risks and uncertainties, including those described below, that we believe apply to our business and the industry in which we operate. You should carefully consider these risks, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described below could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business.

Risks Related to Our Limited Operating History, Business, Financial Condition, Results of Operations, and Need for Additional Capital

We have a limited operating history, have not completed any clinical trials, have no products approved for commercial sale, and have not generated any revenue, which may make it difficult for you to evaluate our current business and likelihood of success and viability.

We are a clinical-stage biotechnology company with a limited operating history with which investors can evaluate our business and prospects. We commenced operations in August 2017, have not completed any clinical trials, have no products approved for commercial sale and have never generated any revenue, and our operations to date have been primarily limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking preclinical studies, preparing for and initiating our first clinical trial, and establishing arrangements with third parties for the manufacture of initial quantities of product candidates. We are currently conducting a Phase 1 clinical trial of our lead product candidate, BMF-219, in adult patients with relapsed or refractory acute leukemia including those with an MLL/KMT2A gene rearrangement or NPM1 mutation, as well as in adult patients with MM, DLBCL and a subset of patients with CLL. In October of 2022, we announced FDA clearance of the IND application for BMF-219 in KRAS mutant solid tumors and the initiation of a Phase 1/1b clinical trial (COVALENT-102). In October 2022, we announced the completion of the Phase 1 portion of COVALENT-111 in healthy volunteers in Canada and the dosing of the first patient with type 2 diabetes in the Phase 2 portion of COVALENT-111, also in Canada. In December 2022, we announced the clearance of the IND by the FDA to evaluate BMF-219 in type 2 diabetes mellitus in COVALENT-111 at sites in the U.S..

We have not demonstrated an ability to successfully conduct or complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a company with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We have not yet demonstrated an ability to successfully overcome such risks and difficulties, or to make such a transition. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We expect our financial condition and results of operations to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have incurred significant net losses in each period since our inception, and we expect to incur significant net losses for the foreseeable future.

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We are early in our development efforts and have not yet completed the development of any of our product candidates. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. Even if we succeed in receiving marketing approval for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to discover, develop and market additional potential products. We have financed our operations primarily through sales of our common stock and convertible preferred stock.

We have incurred significant net losses in each reporting period since we commenced operations in August 2017. Our net losses were $81.8 million and $41.6 million, for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $131.6 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- continue our research and development efforts and submit additional INDs;
- conduct preclinical studies and clinical trials, including our ongoing Phase 1 clinical trial of BMF-219 in various types of liquid and solid tumors, our ongoing Phase 1/2 clinical trial of BMF-219 in type 2 diabetes, and our IND-enabling studies for BMF-500;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges;
- establish a sales, marketing, and distribution infrastructure and scale-up manufacturing capabilities, whether alone or with third parties, to commercialize any product candidates for which we may obtain regulatory approval, if any;
- obtain, expand, maintain, enforce, and protect our intellectual property portfolio;
- hire additional clinical, regulatory, and scientific personnel; and
- operate as a public company.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop, seek regulatory approval for and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We have not generated any revenue from our product candidates and may never generate revenue or be profitable. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery and development of our product candidates.

Our ability to become profitable depends upon our ability to generate revenue. We have not received marketing approval for any product candidate, and we have not generated any revenue from any product sales or other sources since our inception. We do not expect to generate revenue unless or until we successfully complete preclinical and clinical development and obtain regulatory approval of, and then successfully commercialize, at least one product candidate. BMF-219, our lead product candidate, is in the early stage of clinical development. As such, we face significant translational risk as our product candidates advance further in clinical development, and promising results in preclinical studies or early clinical trials may not be replicated in later-stage clinical trials. All of our current and future product candidates will require preclinical and clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity, and significant marketing efforts before we can generate any revenue from product sales. Our ability to generate revenue depends on a number of factors, including, but not limited to:

- timely initiation and completion of our preclinical studies and clinical trials for BMF-219, BMF-500 and our future product candidates, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- establishing and maintaining relationships with contract research organizations (CROs) and clinical sites for the ongoing clinical development of BMF-219 and future clinical development of BMF-500 and any future product candidates;
- our ability to complete IND-enabling studies, including for BMF-500, and successfully submit and receive authorization to proceed under INDs or comparable applications;

- whether we are required by the FDA or other comparable foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- our ability to demonstrate to the satisfaction of the FDA and comparable foreign regulatory authorities the safety, efficacy, consistent manufacturing quality, and acceptable risk-benefit profile of our small molecule product candidates or any future product candidates;
- the prevalence, duration, and severity of potential side effects or other safety issues experienced with our product candidates or future product candidates, if any;
- the timely receipt of necessary regulatory approvals from the FDA and comparable foreign regulatory authorities;
- the willingness of physicians, operators of clinics, and patients to utilize or adopt any of our product candidates or future product candidates over alternative or more conventional therapies, such as chemotherapy, to treat various types of cancer;
- the actual and perceived availability, cost, risk profile and side effects and efficacy of our product candidates, if approved, relative to existing and future alternative therapies in our target indications, including cancer and metabolic diseases, and competitive product candidates and technologies;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate and maintain commercially viable manufacturing processes that are compliant with cGMP;
- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the United States and internationally, if approved for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- patient demand for our current product candidates and any future product candidates, if approved;
- our ability to establish and enforce intellectual property rights in and to our product candidates or any future product candidates;
- obtaining coverage and adequate reimbursement by third-party payors for our product candidates;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring, and retaining qualified personnel.

Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing our product candidates. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the sale of our product candidates or any future product candidates, we may be unable to continue operations without continued funding.

Due to the significant resources required for the development of our product candidates, we must prioritize development of certain product candidates and/or certain indications. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We are currently focused on the discovery and development of novel covalent small molecules to treat patients with genetically defined cancers and metabolic diseases. We seek to maintain a process of prioritization and resource allocation among our programs to maintain a balance between advancing our lead product candidate, BMF-219, as well as developing our other and any future product candidates, including BMF-500.

Our decisions concerning the allocation of research, development, collaboration, management, and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities with other therapeutic platforms or product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaboration, licensing or other royalty arrangements in cases in which it

would have been more advantageous for us to retain sole development and commercialization rights. In addition, if we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the cancer or metabolic disease treatment landscape or in the pharmaceutical, biopharmaceutical or biotechnology industry more generally, our business, financial condition and results of operations could be materially adversely affected.

We will require substantial additional capital to finance our operations and we will not be able to continue as a going concern if we are unable to do so. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and product development programs or future commercialization efforts.

Since our inception, we have used substantial amounts of cash to fund our operations, and our expenses will increase substantially in the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development of, initiate and conduct clinical trials of, and seek marketing approval for our product candidates. Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed significant amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek marketing approval for, BMF-219, and advance our future product candidates. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing, and distribution activities. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies to perform preclinical studies or clinical trials in addition to those that we currently anticipate. Other unanticipated costs may also arise. Because the design and outcome of our ongoing and planned clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of any product candidate we develop. We also expect to incur additional costs associated with our continuing operation as a public company. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

As of December 31, 2022, we had $113.4 million in cash, cash equivalents, restricted cash, and investments. Based on our current operating plan, we believe that our existing cash and cash equivalents, restricted cash, and investments as of December 31, 2022, without any future financing, will not be sufficient for the Company to continue as a going concern for at least one year from the issuance date of the financial statements appearing elsewhere in this Annual Report on Form 10-K. Our estimate as to how long we expect our existing capital resources to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Such financing may dilute our stockholders or restrict our operating activities. To the extent we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments and engage in certain merger, consolidation, or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license to others rights to our product candidates in certain territories or indications that we would prefer to develop and commercialize ourselves. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we raise additional funds through upfront payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to our product candidates or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future capital requirements depend on many factors, including but not limited to:

- the scope, timing, progress, duration, costs and results of our clinical trials, drug discovery, preclinical development activities, and laboratory testing for our product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the extent to which we discover and develop additional product candidates;

- the cost, timing, and outcome of regulatory review of our product candidates;
- the cost and timing of establishing sales and marketing capabilities, if any of our product candidates receive marketing approval;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- licensing, or other arrangements into which we may enter in the future, including the timing of receipt of any milestone or royalty payments under these agreements;
- the timing, receipt, and amount of sales from our potential products;
- our need and ability to hire additional management, scientific, and medical personnel;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems;
- our efforts to enhance operational systems and our ability to attract, hire, and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company;
- the cost associated with commercializing our product candidates, if they receive regulatory approval;
- our ability to establish and maintain strategic collaborations and other similar partnerships for the development and commercialization of our product candidates; and
- the impact of the ongoing COVID-19 pandemic and adverse global economic conditions on our business, which may exacerbate the magnitude of the factors discussed above.

We do not have any committed external source of funds and adequate additional financing may not be available to us on acceptable terms, or at all. In addition, our ability to raise additional capital may be adversely impacted by potential worsening global economic and political conditions, inflationary pressures, increases in interest rates and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic or other factors.

There is substantial doubt about our ability to continue as a going concern.

To date, we have not generated any revenues from product sales and have incurred significant operating losses in each year since our inception and we anticipate that losses may continue for the next several years or until such time as we can generate substantial revenues and achieve profitability. In connection with the preparation of this Annual Report for the year ended December 31, 2022, our management has concluded that there is substantial doubt as to whether we can continue as a going concern for the twelve months following the issuance of this Annual Report. Our ability to continue as a going concern is dependent upon raising capital to maintain current operations and continue research and development efforts. We plan to raise additional capital to fund our operations through public or private equity offerings, debt financings, and/or potential collaborations and license arrangement or other sources. There is no assurance, however, that any additional financing or any revenue-generating collaboration will be available when needed or that we will be able to obtain financing or enter into a collaboration on terms acceptable to us.

Based on our current operating plan, we will not be able to continue as a going concern over the next twelve months unless we raise additional capital by other means. These factors raise substantial doubt about our ability to continue as a going concern.

Recent volatility in capital markets and lower market prices for many securities may affect our ability to access new capital through sales of shares of our common stock or issuance of indebtedness, which may harm our liquidity, limit our ability to grow our business, pursue acquisitions or improve our operating infrastructure and restrict our ability to compete in our markets.

Our operations consume substantial amounts of cash, and we intend to continue to make significant investments to support our business growth, pursue the preclinical and clinical development of our product candidates, respond to business challenges or opportunities, retain or expand our current levels of personnel, enhance our operating infrastructure, and

potentially acquire complementary businesses and technologies. Our future capital requirements may be significantly different from our current estimates and will depend on many factors, including the need to:

- finance unanticipated working capital requirements;
- develop or enhance our technological infrastructure and our existing research and development capabilities;
- pursue acquisitions or other strategic relationships; and
- respond to competitive pressures.

Accordingly, we may need to pursue equity or debt financings to meet our capital needs. With uncertainty in the capital markets and other factors, such financing may not be available on terms favorable to us or at all. If we raise additional funds through further issuances of equity or convertible debt securities, our existing stockholders could suffer significant dilution, and any new equity securities we issue could have rights, preferences, and privileges superior to those of holders of our common stock. Any debt financing secured by us in the future could require us to pay significant interest on borrowings or involve additional restrictive covenants relating to our capital-raising activities and other financial and operational matters, which may make it more difficult for us to obtain additional capital and to pursue business opportunities, including potential acquisitions. Our inability to obtain adequate financing or financing on terms satisfactory to us could have a negative impact on our financial condition and we could face significant limitations on our ability to pursue our business strategies, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical trials or future commercialization efforts.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults, or non-performance by financial institutions or transactional counterparties, could adversely affect the Company's current and projected business operations and its financial condition and results of operations.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank ("SVB") was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. If any of our suppliers or other parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected. In this regard, counterparties to SVB credit agreements and arrangements, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure of SVB and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008-2010 financial crisis.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect the Company, the financial institutions with which we have or may enter into credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or

financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions with which we have or may enter into financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Delayed or lost access to working capital sources and/or delays, inability or reductions in our ability to enter into new credit facilities or access other working capital resources;
- Potential or actual breach of contractual obligations that require the Company to maintain letters of credit or other credit support arrangements; or
- Potential or actual breach of financial covenants in any credit agreements or credit arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws and otherwise have a material adverse impact on our business.

Risks Related to Product Development

Our discovery and development activities are focused on the development of novel covalent small molecule therapies, initially targeted at menin, to treat patients with genetically-defined cancers and metabolic diseases, and the approach we are taking to discover and develop such product candidates is novel, may never lead to marketable products and may not ultimately represent a significant market.

The discovery and development of covalent small molecule therapies for patients with genetically-defined cancers and metabolic diseases, with a particular focus on menin, is an emerging field. While there is scientific evidence to support the feasibility of developing covalent therapies, the significant complexity and potential safety and toxicity concerns associated with poorly designed covalent binders have historically discouraged drug developers from pursuing this drug class. In particular, a significant risk for toxicity is posed by these small-molecule covalent binders if they demonstrate a more promiscuous binding profile than intended, which can potentially cause unacceptable levels of off-target interactions. While we believe the significant expertise, foundational knowledge and capabilities that our management team members have accumulated over their extensive careers and that we have expanded and refined since our inception positions us to overcome such challenges, there can be no assurance that we will be successful. Even if we are able to limit off-target interaction, there can be no assurance that treatment with any of our novel covalent small molecule product candidates will demonstrate the deep inactivation of their targets or offer greater therapeutic windows than conventional non-covalent drugs. It is possible that the targets we select, such as menin, could be effectively and safely treated by more frequent dosing of non-covalent drugs, which could limit the potential advantages or perceived benefits of our covalent inhibitor product candidates.

Furthermore, although we believe, based on our preclinical work and research on covalent binders generally, that highly selective covalent inhibitors of certain critically important oncogenic drivers, such as menin, known to impact cellular processes have potential as precision oncology targets, clinical results may not confirm this hypothesis or may only confirm it for certain inhibitors or certain tumor types.

In addition, our lead product candidate, BMF-219, is in clinical development, and our current data is limited to animal models and preclinical cell lines, the results of which may not translate into humans. As such, even if we are able to develop small-molecule therapies that demonstrate positive results in preclinical studies there can be no assurance that such product candidates will subsequently demonstrate significant clinical benefit *in vivo* or be well-tolerated.

Further, even if our approach is successful in demonstrating the clinical benefit of using our lead product candidate, BMF-219, which is designed to be a highly active and selective covalent inhibitor of menin, in certain menin-driven cancers and/or metabolic diseases, we may never successfully identify additional covalent binding product candidates to validated oncology

or other targets through our FUSION™ System. Therefore, we do not know if our approach of treating patients with genetically-defined cancers and metabolic diseases will be successful, and if our approach is unsuccessful, our business will be materially adversely affected.

Our novel approach to the discovery and development of our current and future product candidates is unproven, and we may not be successful in our efforts to use and expand our FUSION™ System to build a pipeline of product candidates with commercial value.

A key element of our strategy is to utilize our FUSION System to build a pipeline of novel covalent small molecule product candidates and progress these product candidates through clinical development for the treatment of various cancers and metabolic diseases. Although our research and development efforts to date have resulted in our discovery and preclinical development of BMF-219, BMF-500 and other programs, BMF-219, BMF-500 and such other programs may not be safe or effective in our target indications, and we may not be able to further develop BMF-219, BMF-500 or any future product candidates. Our FUSION System is unproven and may not enable us to build a pipeline of product candidates. For example, we may not be successful in identifying validated and novel targets that are amenable to direct intervention with a covalent binder, we may not succeed in creating novel chemical scaffolds to exploit target proteins and we may not be able to maximize the selectivity, potency and safety of our covalent small molecules. There can be no assurance that any development problems we experience in the future related to our platform will not cause significant delays or unanticipated costs or that such development problems can be solved. Even if we are successful in building our pipeline of product candidates, the potential product candidates that we identify may not be suitable for clinical development or generate acceptable clinical data, including as a result of being shown to have unacceptable toxicity or other characteristics that indicate that they are unlikely to be products that will receive marketing approval from the FDA or other regulatory authorities or achieve market acceptance. Furthermore, if one or more of our covalent small molecule product candidates generally proves to be ineffective, unsafe or commercially unviable, the development of our entire platform and pipeline utilizing our FUSION System could be delayed, potentially permanently.

Even if our product candidates are successful in inhibiting certain protein binding, such success would not provide a guarantee of the effectiveness of such product candidate in total tumor regression *in vivo*. For example, even if BMF-219 demonstrates an ability to inhibit menin *in vivo*, there can be no assurance that such inhibition will provide significant clinical benefit when evaluated in humans.

In addition, development of covalent small molecules is highly complex and we may experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to manufacturing partners, which may prevent us from initiating or completing our planned clinical trials or commercializing any products we develop on a timely or profitable basis, if at all. In addition, since we have not yet entered clinical development, we do not know the specific doses that may be effective in the clinic or, if approved, commercially. Finding a suitable dose may delay our anticipated clinical development timelines.

If we do not successfully develop and commercialize product candidates, we will not be able to generate product revenue which could materially adversely affect our business, financial condition and results of operations.

We are very early in our development efforts and are substantially dependent on our lead product candidate, BMF-219. If we are unable to advance BMF-219 or any other product candidates through clinical development, obtain regulatory approval and ultimately commercialize BMF-219 or any other product candidates, or experience significant delays in doing so, our business, financial condition and results of operations will be materially adversely affected.

We are early in our development efforts. We have not yet successfully completed clinical testing of our lead product candidate, BMF-219, in human subjects, and we have only selected one additional development candidate, BMF-500, from our other two covalent small molecule programs. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization of BMF-219, BMF-500, and one or more of our future product candidates. The success of our product candidates will depend on several factors, including the following:

- our ability to continue our business operations and product candidate research and development, and adapt to any changes in the regulatory approval process, manufacturing supply or clinical trial requirements and timing due to the ongoing COVID-19 pandemic and otherwise, including complying with new regulatory guidance or requirements on conducting clinical trials during the ongoing COVID-19 pandemic;
- successful completion of preclinical studies;

- receipt of authorization to proceed under INDs for our planned clinical trials or future clinical trials;
- successful initiation, patient enrollment in, and completion of clinical trials, including our ongoing Phase 1 clinical trial of BMF-219 in various types of liquid tumors, our Phase 1/1b clinical trial of BMF-219 in various types of solid tumors, and our Phase 1/2 clinical trial of BMF-219 in type 2 diabetes mellitus, which may be impacted by the ongoing COVID-19 pandemic;
- whether BMF-219, BMF-500 or any other product candidates that we may identify and pursue will demonstrate safety, tolerability and efficacy profiles that are satisfactory to the FDA or any foreign regulatory authority for marketing approval;
- receipt of marketing approvals for our product candidates from applicable regulatory authorities;
- completion of any required post-marketing approval commitments to applicable regulatory authorities in order to maintain marketing authorization for any of our product candidates that receive regulatory approval;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates, if any product candidates are approved;
- establishing sales, marketing, and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies for cancer or metabolic diseases;
- obtaining and maintaining third-party coverage and adequate reimbursement; and
- maintaining a continued acceptable safety profile of our products following approval.

Many of these factors are beyond our control, and it is possible that we may never obtain regulatory approval for our product candidates even if we expend substantial time and resources seeking their development and approval. If we do not achieve regulatory approval in a timely manner or at all, we could experience significant delays or an inability to commercialize our current or future product candidates, which would materially adversely affect our business. If we do not receive regulatory approvals for our current or future product candidates, we will not be able to continue our operations.

The success of our business, including our ability to finance our company and generate revenue from products in the future, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and eventual commercialization of the product candidates we develop, which may never occur. Our current product candidates, and any future product candidates we develop, will require additional preclinical and clinical development, management of clinical, preclinical and manufacturing activities, marketing approval in the United States and other markets, demonstrating cost-effectiveness to pricing and reimbursement authorities, obtaining sufficient manufacturing supply for both clinical development and commercial production in accordance with cGMP, building of a commercial organization, and substantial investment and significant marketing efforts before we generate any revenue from product sales, if ever. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our preclinical studies or clinical trials or commercializing our product candidates on a timely or profitable basis, if at all. Changes in the manufacturing process or facilities will require further comparability analysis and approval by FDA before implementation, which could delay our preclinical studies, clinical trials and product candidate development, and could require additional preclinical studies and clinical trials, including bridging studies, to demonstrate consistent and continued safety and efficacy.

We have not previously submitted an NDA to the FDA or similar approval filings to a comparable foreign regulatory authority, for any product candidate. An NDA or other relevant regulatory filing must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product. We cannot be certain that our current or future product candidates will be successful in clinical trials or receive regulatory approval. Further, even if they are successful in clinical trials, our product candidates or any future product candidates may not receive regulatory approval. If we do not receive regulatory approvals for current or future product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a product candidate, our revenue will depend, in part, upon the size of the markets in the

territories for which we gain regulatory approval and have commercial rights for each product candidate, as well as the availability of competitive products, whether there is sufficient third-party reimbursement and adoption by physicians.

Preclinical and clinical drug development is a lengthy and expensive process, with an uncertain outcome. Our preclinical and clinical programs may experience delays or may never be initiated or completed, which would adversely affect our ability to obtain regulatory approvals or commercialize our product candidates on a timely basis or at all, which could have an adverse effect on our business.

In order to obtain FDA approval to market a new small molecule product, we must demonstrate the safety and efficacy of our product candidates in humans to meet the FDA requirements. To meet these requirements, we will have to conduct adequate and well-controlled clinical trials. Clinical testing is expensive, time-consuming, and subject to uncertainty. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical studies that support our planned and future INDs in the United States. At present, we only have one product candidate, BMF-219, in clinical development and have selected only one additional development candidate from our other two covalent small molecule programs. We cannot be certain of the timely completion or outcome of our preclinical studies and cannot predict if the FDA will allow our proposed clinical programs to proceed or if the outcome of our preclinical studies will ultimately support further development of our programs. Our lead product candidate, BMF-219, is in clinical development in selected liquid tumors, solid tumors, and type 2 diabetes, and we cannot be sure that we will be able to submit INDs or similar applications with respect to additional indications or other product candidates on the timelines we expect, if at all, and we cannot be sure that submission of IND or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Conducting preclinical testing and clinical trials represents a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. Delays associated with programs for which we are directly conducting preclinical studies may cause us to incur additional operating expenses. The commencement and rate of completion of preclinical studies and clinical trials for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient preclinical or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- timely completion of preclinical laboratory tests, animal studies and formulation studies in accordance with the FDA's GLP requirements and other applicable regulations;
- approval by an independent IRB ethics committee at each clinical site before each trial may be initiated;
- delays in reaching a consensus with regulatory agencies on study design and obtaining regulatory authorization to commence clinical trials;
- delays in reaching agreement on acceptable terms with prospective CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in recruiting suitable patients to participate in our clinical trials;
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory authorities;
- developments on trials conducted by competitors for related technology that raises FDA or foreign regulatory authority concerns about risk to patients of the technology broadly, or if the FDA or a foreign regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in recruiting, screening and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties or us to adhere to clinical trial protocols;
- failure to perform in accordance with the FDA's or any other regulatory authority's GCPs, or applicable regulatory guidelines in other countries;

- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in trial of the same class of agents conducted by other companies;
- changes to the clinical trial protocols;
- clinical sites deviating from trial protocol or dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization (CMO), and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

In addition, disruptions caused by the ongoing COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing preclinical studies and clinical trials. Any inability to successfully initiate or complete preclinical studies or clinical trials could result in additional costs to us or impair our ability to generate revenue from product sales. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products, if and when approved, have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may seriously harm our business.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Delays in the completion of any preclinical studies or clinical trials of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our preclinical studies or clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

The results of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or other comparable foreign regulatory authorities. Successful preclinical studies and clinical trials cannot provide assurance of successful commercialization.

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective before we can seek regulatory and marketing approvals for their commercial sale. Success in preclinical studies does not mean that future clinical trials will be successful. For instance, we do not know whether BMF-219 will perform in clinical trials as BMF-219 has performed in preclinical studies, nor can we predict how our future product candidates will perform in future preclinical studies or clinical trials. Product candidates in later-stage clinical trials

may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and other comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety, which could delay regulatory approval, limit the size of the patient population to which we may market our product candidates or prevent regulatory approval. In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our product candidates may also be undergoing surgical, radiation and chemotherapy treatments and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our product candidates. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes.

The ongoing COVID-19 pandemic could materially adversely impact our business, results of operations, and financial condition, including our preclinical studies and clinical trials.

The ongoing COVID-19 pandemic and government responses have created disruptions in global supply chains and have continued to adversely impact many industries. The ongoing pandemic could have a continued material adverse impact on economic and market conditions and trigger a period of global economic slowdown. We continue to monitor the impact of the ongoing COVID-19 pandemic closely. The extent to which the ongoing COVID-19 pandemic will impact our operations or financial results is uncertain.

The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the continued spread of COVID-19, we have our administrative employees complying with state and county COVID-19 guidelines and protocols when working in our offices and limited the number of staff in any given research and development laboratory. Our research and development teams are currently operating on a staggered schedule, which has altered our operations and processes. While the extent of the impact of the ongoing COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health emergency such as the ongoing COVID-19 pandemic could have a material adverse effect on our business, financial condition and results of operations. As a result of the ongoing COVID-19 pandemic, we may experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- interruptions in preclinical studies due to restricted or limited operations at our laboratory facility;
- delays or difficulties in clinical site initiation, including difficulties in recruiting CROs for our preclinical studies and clinical site investigators and clinical site staff for our ongoing and planned clinical trials;
- delays or difficulties in enrolling and retaining patients in our ongoing and planned clinical trials;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our CMOs due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- interruptions or delays to our sourced discovery and clinical activities; and
- changes in clinical site procedures and requirements as well as regulatory requirements for conducting clinical trials during the pandemic.

We may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the SARS-CoV-2 virus. For example, in March 2020, the FDA issued a guidance, which the FDA subsequently revised, on conducting clinical trials during the pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic. In addition, since the beginning of the COVID-19 pandemic, multiple vaccines for COVID-19 have received Emergency Use Authorization by the FDA and some of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials.

The continued extent to which the COVID-19 pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the emergence and impact of variants, plateaued or stagnant booster rates, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

The trading prices for shares of other biopharmaceutical companies have been highly volatile as a result of the ongoing COVID-19 pandemic and the trading prices for shares of our common stock could also experience high volatility. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression, or other sustained adverse market event resulting from the spread of COVID-19 could materially and adversely affect our business and the value of our common stock.

We have not experienced delays in our discovery and development activities as a result of the ongoing COVID-19 pandemic, but may in the future if some of our CROs and other service providers are impacted. In addition, the ultimate impact of the ongoing COVID-19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments, which cannot be accurately predicted, including the duration of the pandemic, the ultimate geographic spread of the disease, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and any future variants and the actions taken to contain COVID-19 or address its impact in the short and long term, among others. We do not yet know the full extent of potential delays or impacts on our business, our preclinical studies or planned clinical trials, our research programs, healthcare systems or the global economy. We will continue to monitor the situation closely.

In addition, our business could be materially adversely affected by other business disruptions to us or our third-party providers that could materially adversely affect our potential future revenue and financial condition and increase our costs and expenses. Our operations, and those of our CROs, CMOs, and other contractors, consultants, and third parties could be subject to other global pandemics, earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could materially adversely affect our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

To the extent that the ongoing COVID-19 pandemic adversely affects our business, financial condition, and operating results, it may also have the effect of heightening many of the risks described in this “Risk Factors” section.

If we experience delays or difficulties in the enrollment and/or retention of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue our ongoing and planned clinical trials on a timely basis or at all for our product candidates if we are unable to recruit and enroll a sufficient number of eligible patients to participate in these trials through completion of such trials as required by the FDA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

Our clinical trials will compete with other clinical trials that are in the same therapeutic areas as our product candidates, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified

clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. In addition, there may be limited patient pools from which to draw for clinical studies. In addition to the rarity of some diseases, particularly certain cancer indications, the eligibility criteria of our clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. Patient enrollment for our ongoing and planned clinical trials may be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs or other methods of treatment for the disease under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol;
- perceived risks and benefits of the product candidate under study;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or future product candidates being investigated for the indications we are pursuing;
- clinicians' willingness to screen their patients for biomarkers to indicate which patients may be eligible for enrollment in our clinical trials;
- delays in or temporary suspension of the enrollment of patients in our planned clinical trials due to the ongoing COVID-19 pandemic;
- ability to obtain and maintain patient consents;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion, including as a result of contracting COVID-19 or other health conditions or being forced to quarantine, or, because they may be late-stage cancer patients, will not survive the full terms of the clinical trials.

These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods.

The market opportunities for our product candidates may be relatively small as it will be limited to those patients who are ineligible for or have failed prior treatments and our estimates of the prevalence of our target patient populations may be inaccurate.

Cancer therapies are sometimes characterized as first line, second line, or third line, and the FDA customarily approves new therapies only for a second line or later lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapies, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect to initially seek approval of our product candidates in second or later lines of therapy. Subsequently, depending on the nature of the clinical data and experience with any approved products or product candidates, if any, we may pursue approval as an earlier line therapy and potentially as a first line therapy. There is no guarantee, however, that our product candidates that we may identify and pursue, even if approved as a second or subsequent line of therapy, would be approved for an earlier line of therapy, and, prior to seeking any such approvals, we may have to conduct additional clinical trials.

The incidence and prevalence for target patient populations of BMF-219 and BMF-500 are based on estimates and third-party sources. If the market opportunities for BMF-219, BMF-500 or any future product candidate we may develop, if and when approved, are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability might be materially and adversely affected.

Periodically, we make estimates regarding the incidence and prevalence of target patient populations for particular diseases based on various third-party sources and internally generated analysis and use such estimates in making decisions regarding our drug development strategy, including acquiring or in-licensing product candidates and determining indications on which to focus in nonclinical or clinical trials.

The incidence and prevalence for target patient populations of BMF-219 and BMF-500 are based on estimates and third-party sources. These estimates may be inaccurate or based on imprecise data. For example, the total addressable market opportunity will depend on, among other things, acceptance of our drugs by the medical community and patient access, drug pricing and reimbursement. The number of patients in the addressable markets may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, or new patients may become increasingly difficult to identify or gain access to. If the market opportunities for BMF-219, BMF-500 or any future product candidate we may develop, if and when approved, are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability might be materially and adversely affected.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, intense competition and a strong emphasis on intellectual property. We believe that our approach, strategy, scientific capabilities, know-how and experience provide us with competitive advantages. In addition, we believe we are currently the only company in the United States developing covalent small molecule product candidates specifically targeted against menin. More broadly, we define ourselves as targeted drug developers focused on covalent small molecule therapeutics and as such expect substantial competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions and governmental agencies and public and private research institutions worldwide. Many of our competitors, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies may be or may become interested in discovery and development of covalent binders that may compete with us against menin or related targets at scale and in an integrated way. Even if they do not advance programs with the same mechanism of action as ours, these companies could develop products or product candidates that are competitive with ours or that have a superior product profile, and may do so at a rapid pace. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do. We face competition from segments of the pharmaceutical, biotechnology and other related markets that pursue the development of therapies that target covalent binding against protein targets of interest to us.

In particular, we are aware of Kura Oncology's KO-539 and Syndax Pharmaceuticals' SNDX-5613, both of which target menin through the use of non-covalent inhibition. Both KO-539 and SNDX-5613 are in clinical development and have demonstrated Phase 1 results that support continued development into pivotal studies and validate menin as a therapeutic target. Other clinical programs have been reported by Daiichi Sankyo (DS-1594), Janssen Pharmaceuticals (JNJ-75276617) and Sumitomo Pharma Oncology (DSP-5336). Additionally, other preclinical programs have been reported by Bayer (BAY-155), Novartis, and the University of Michigan.

We face competition with respect to our current product candidates and will face competition with respect to future product candidates, from segments of the pharmaceutical, biotechnology, and other related markets that pursue targeted therapies for patients with genetically-defined cancers and metabolic diseases. Our competitors will also include companies that are or will be developing other targeted therapies, including small molecule, antibody, or protein degraders for the same indications that we are targeting. If BMF-219, BMF-500 or our future product candidates do not offer sustainable advantages over competing products, we may otherwise not be able to successfully compete against current and future competitors.

Our competitors may obtain regulatory approval of their product candidates more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products.

Our competitors will also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Furthermore, we also face competition more broadly across the market for cost-effective and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy or a combination of such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic, including branded generic, products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market will pose challenges. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

Product candidates that we may successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their potency, selectivity, inactivation of the target, therapeutic window, safety, convenience, price, the level of generic competition, our ability to market and commercialize the product candidate and the availability of reimbursement from government and other third-party payors. For additional information regarding our competition, see the section of this Annual Report on Form 10-K titled “Business—Competition.”

Our covalent small molecule product candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may adversely affect our business, financial condition and prospects significantly.

As is the case with all oncology drugs, it is likely that there may be significant side effects associated with their use. BMF-219, BMF-500 or future product candidates may be used in populations for which safety concerns may be reviewed by regulatory agencies. For example, if the administration of BMF-219 leads to levels of menin inhibition that far exceed those achieved by well-studied non-covalent menin inhibitors, it is possible that patients' responses could be both unexpected and negative. In addition, we or our future collaborators may study BMF-219 in combination with other therapies, which may exacerbate adverse events associated with the therapy. Further, our product candidates will be used in patients that have weakened immune systems, which may exacerbate any potential side effects associated with their use. Patients treated with BMF-219, BMF-500 or any of our future product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or adverse events that are unrelated to our product candidate but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients’ illnesses. For example, it is expected that some of the patients enrolled in our clinical trials of BMF-219 will die or experience major clinical events either during the course of our clinical trials or after participating in such trials. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects.

If further significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially adversely affect our business, financial condition and prospects.

Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates previously not seen during clinical testing may also develop after such approval and lead to a number of potentially significant negative consequences, including, but not limited to:

- regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including "boxed" warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a risk evaluation and mitigation strategy (REMS), which could include a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business.

Interim, "top-line", and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we have announced or published, and may continue to publicly disclose, preliminary or top-line data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could materially adversely affect our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in

general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be adversely affected, which could materially adversely affect our business, financial condition and results of operations.

Even if we obtain regulatory approval of our product candidates, the products may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers and others in the medical community.

The use of precision medicines as a potential cancer treatment is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers and others in the medical community. Various factors will influence whether our product candidates, if approved, are accepted in the market, including:

- the clinical indications for which our product candidates are approved;
- physicians, hospitals, cancer treatment centers, and patients considering our product candidates as a safe and effective treatment;
- the potential and perceived advantages of our product candidates over alternative treatments;
- our ability to demonstrate the advantages of our product candidates over other cancer medicines;
- the prevalence and severity of any side effects;
- the prevalence and severity of any side effects for other precision medicines and public perception of other precision medicines;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA;
- the timing of market introduction of our product candidates as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- pricing and the availability of adequate coverage and reimbursement by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

If our product candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue.

In addition, although our product candidates differ in certain ways from other precision medicine approaches, serious adverse events or deaths in other clinical trials involving precision medicines, even if not ultimately attributable to our product or product candidates, could result in increased government regulation, unfavorable public perception and publicity, potential regulatory delays in the testing or licensing of our product candidates, stricter labeling requirements for those product candidates that are licensed, and a decrease in demand for any such product candidates.

Even if any products we develop achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

Coverage and reimbursement of newly-approved products from third-party payors is uncertain. Our product candidates may become subject to unfavorable pricing regulations and/or third-party coverage and reimbursement policies, either of which would adversely affect our business. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy products. Sales of these or future product candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our product candidates. For additional information, see the section of this Annual Report on Form 10-K titled "Business—Coverage and Reimbursement."

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may materially change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third-party payors for any approved products that we develop could have a material adverse effect on our business, financial condition and results of operations, our ability to raise capital needed to commercialize products and our overall financial condition.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

If product liability lawsuits are brought against us, we may incur substantial liabilities, which may not be sufficiently covered by insurance, and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the planned clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are

perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants
- initiation of investigations by regulators;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Although we have clinical trial insurance that we believe is appropriate for our stage of development, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage and may need to obtain higher levels prior to marketing any of our product candidates if approved. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition.

We have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators.

We have never commercialized a product candidate and we currently have no sales force, marketing or distribution capabilities. To achieve commercial success for the product candidates which we may license to others, we will rely on the assistance and guidance of those collaborators. For product candidates for which we retain commercialization rights and marketing approval, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party.

Factors that may affect our ability to commercialize our product candidates, if approved, on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, developing adequate educational and marketing programs to increase public acceptance of our product candidates, ensuring regulatory compliance of our company, employees and third parties under applicable healthcare laws and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization will be expensive and time-consuming and could delay the launch of our product candidates upon approval. We may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may not generate revenue from them or be able to reach or sustain profitability.

Risks Related to Regulatory Process and Other Legal Compliance Matters

The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including our lead product candidate BMF-219, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for each targeted indication.

Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval.

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations or changes in regulatory review for each submitted IND, NDA or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials or require us to modify the design of our clinical trials, including additional procedures and contingency measures in response to the ongoing COVID-19 pandemic or as required by clinical sites, IRBs, the FDA or other regulatory authorities;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks, or that a product candidate has an acceptable benefit-risk ratio for its proposed indication;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures, specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- our third-party contractors may fail to comply with regulatory requirements or otherwise fail or be unable to adequately perform their obligations to allow for the conduct of our planned or future clinical studies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical

trial results may result in our failing to obtain regulatory approval to market our product candidates, which would materially adversely affect our business, results of operations and prospects.

The FDA or a comparable foreign regulatory authority may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request (including failing to approve the most commercially promising indications), may grant approval contingent on the performance of costly post-marketing clinical studies, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

We may not be able to obtain orphan drug designation or obtain or maintain the benefits associated with orphan drug designation, such as orphan drug exclusivity and, even if we do, that exclusivity may not prevent the FDA or other comparable foreign regulatory authorities, from approving competing products.

As part of our business strategy, we may seek orphan drug designation (ODD) for any eligible product candidates we develop, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing and making available the drug will be recovered from sales in the United States. Our target indications may include diseases with large patient populations or may include orphan indications. However, there can be no assurances that we will be able to obtain orphan designations for our product candidates.

In the United States, ODD entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product that has ODD subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity in instances of supply issues.

Even if we obtain ODD for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained ODD for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process.

A Breakthrough Therapy designation or Fast Track designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive regulatory approval in the United States.

We may seek Breakthrough Therapy designation for some of our product candidates. A Breakthrough Therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Products designated as Breakthrough Therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates

meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as Breakthrough Therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We may seek Fast Track designations for some of our product candidates. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the drug or biologic demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for Fast Track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

Accelerated approval by the FDA, even if granted for our current or any other future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive regulatory approval.

We may seek accelerated approval of our current or future product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA requires that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. Under FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

We may seek priority review designation for one or more of our other product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for any products we develop is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of any products we develop in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential product candidates will be adversely affected.

Changes in funding or disruptions at the FDA, the Securities and Exchange Commission and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of the Securities and Exchange Commission (SEC) and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including for 35 days beginning on December 22, 2018, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities.

Separately, since March 2020, when foreign and domestic inspections of facilities were largely placed on hold due to the ongoing COVID-19 pandemic, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic.

If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Even if we receive regulatory approval of our product candidates, we will be subject to extensive ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries.

Following potential approval of any of our current or future product candidates, the FDA or other comparable regulatory authorities may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the product. The FDA may also require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP requirements, tracking and tracing requirements, good laboratory practice requirements, and good clinical practice requirements, for any clinical trials that we conduct post-approval. Additionally, under FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- fines, warning or untitled letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

In addition, the FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling;

(iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. For additional information, see the section of this Annual Report on Form 10-K titled "Business—Healthcare Reform."

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability. Further, it is possible that additional governmental action is taken in response to the ongoing COVID-19 pandemic.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, if approved. In particular, while the FDA permits the dissemination of truthful and non-misleading information about an approved product, a manufacturer may not promote a product for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. Although physicians may prescribe products for "off-label" uses in the exercise of their independent professional judgment, if we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The government has also imposed consent decrees, corporate integrity agreements or permanent injunctions under which specified promotional conduct must be changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Our employees, independent contractors, consultants, principal investigators, CROs, suppliers, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, principal investigators, CROs, suppliers, and vendors acting for or on our behalf may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, research, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and material adversely affect to our reputation. It is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations.

If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business and may constrain the financial arrangements and relationships through which we research, as well as sell, market and distribute any products for which we

obtain marketing approval. Such laws include, without limitation, federal and state anti-kickback, fraud and abuse, false claims, data privacy and security and physician and other healthcare provider payment transparency laws and regulations. If their operations are found to be in violation of any such laws or any other governmental regulations that apply, they may be subject to significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and imprisonment. For additional information, see the section of this Annual Report on Form 10-K titled "Business—Government Regulation—Other Healthcare Laws."

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom may be compensated in the form of stock or stock options for services provided to us and may be in the position to influence the ordering of or use of our product candidates, if approved, may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

We are or may become subject to stringent and changing laws, regulations, contractual obligations, and other obligations relating to privacy, data protection, and information security. The actual or perceived failure by us or our partners, customers, vendors, third-party payors or other related third parties to comply with such obligations could harm our reputation, subject us to significant fines and liability, or otherwise adversely affect our business.

There are numerous domestic and foreign laws, regulations, and other legal obligations regarding privacy, data protection, and information security, the scope of which is changing and subject to differing applications and interpretations, and which may be inconsistent among jurisdictions or conflict with each other. Privacy, data protection, and information security laws and regulations worldwide are, and are likely to remain, uncertain for the foreseeable future, and the actual or perceived failure to address or comply with them by us or our partners, customers, vendors, or other related third-parties could increase our compliance and operational costs, expose us to regulatory scrutiny, actions, fines and penalties, result in reputational harm, lead to a loss of customers; reduce the use of our products, result in litigation and liability, cause a material adverse impact to business operations or financial results, or otherwise result in material harm to our business.

In addition, U.S. states have begun to enact more and more comprehensive privacy, data protection, and information security laws. By way of example, California's California Consumer Privacy Act (CCPA), which went into effect on January 1, 2020, affords consumers expanded privacy protections. Aspects of the CCPA and its interpretation and enforcement remain uncertain. The potential effects of the CCPA are far-reaching and may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply. For example, the CCPA gives California residents expanded rights to access and require deletion of their personal information, opt-out of certain personal information sharing, and receive detailed information about how their personal information is used.

Additionally, we are or may become subject to the terms of internal and external policies, representations, standards, contractual obligations, and other obligations to third parties related to privacy, data protection, and information security. Our actual or perceived failure to comply with them may cause us to suffer a material adverse impact to our business operations or financial results, or otherwise result in material harm to our business.

In view of applicable privacy, data protection, and information security laws, regulations, and standards imposing complex and burdensome obligations, and with substantial uncertainty in their interpretation and compliance, we have faced and may face challenges in addressing and complying with them, and may expend significant resources in an effort to do so, any of which could result in a material adverse impact to our business operations or financial results, or otherwise result in material harm to our business.

For example, in the United States, most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by HITECH, and their respective implementing regulations. Compliance with HIPAA and HITECH may require us to modify our data processing policies and to incur substantial costs and expenses.

We may in the future receive inquiries or be subject to investigations, proceedings, or actions by governmental entities, or litigation by private parties, regarding our privacy, data protection, and information security practices, which could result in a cause a material adverse impact to our business operations or financial results, or otherwise result in material harm to our business, including without limitation, interruptions of or require changes to our business practices, the diversion of resources and the attention of management from our business, regulatory oversights and audits, discontinuance of necessary data processing, or other remedies that adversely affect our business.

Our research and development activities could be affected or delayed as a result of possible restrictions on animal testing.

Certain laws and regulations require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted, delayed or become more expensive.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Such Trade Laws also govern export controls, as well as economic sanctions and embargoes on certain countries and persons. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We also expect our non-U.S. activities to increase in time. We plan to engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents or partners, even if we do not explicitly authorize or have prior knowledge of such activities. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Risks Related to Employee Matters, Managing Our Growth and Other Risks Related to Our Business

We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including our Chief Executive Officer and Chairman of the Board of Directors, Thomas Butler, and Chief Operating Officer and President, Ramses Erdtmann. We will need to hire additional personnel as we initiate and expand our clinical development and if we initiate commercial activities. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could materially adversely affect our business, financial condition and results of operations. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be adversely affected.

Additionally, we rely on our founders and other scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting relationships with our scientific founders or if they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be materially adversely affected.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2022, we had 83 full-time employees, including 59 employees engaged in research and development activities. In order to successfully implement our development and commercialization plans and strategies, and as we continue to operate as a public company, we expect to need additional managerial clinical, regulatory, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, retaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA, and other comparable foreign regulatory agencies' review process for BMF-219, BMF-500 and any future product candidates, while complying with any contractual obligations to contractors and other third parties we may have; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and, if approved, commercialize BMF-219, BMF-500 and future product candidates will depend, in part, on our ability to effectively manage any future growth in company headcount. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third-party service providers is compromised for any reason, our preclinical studies and clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of BMF-219, BMF-500 or any future product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third-party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize BMF-219, BMF-500 or any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Business disruptions could materially adversely affect our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our CROs, CMOs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, pandemics, and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously adversely affect our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Our ability to develop BMF-219, BMF-500 or any future product candidates we may develop could be disrupted if our operations or those of our suppliers are affected by man-made or natural disasters or other business interruptions. Our

corporate headquarters are located in California near major earthquake faults and fire zones. The ultimate impact on us, our significant suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and business could suffer in the event of a major earthquake, fire or other natural disaster.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be limited.

Our net operating loss (NOL) carryforwards that we generate in the future may be unavailable to offset future taxable income because of restrictions under U.S. tax law. Under current U.S. tax law, our federal NOLs generated in taxable years beginning after December 31, 2020 may be carried forward indefinitely, but such deductibility is limited to 80% of current year taxable income.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change" (generally defined as a cumulative change (by value) in the corporation's ownership by "5-percent shareholders" that exceeds 50 percentage points over a rolling three-year period), the corporation's ability to use its pre-change NOLs and certain other pre-change tax attributes to offset its post-change taxable income or tax liabilities may be limited. Similar rules may apply under state tax laws. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. We have performed a Section 382 study and concluded that our ability to utilize our NOLs and certain other tax attributes could be limited by an ownership change as described above and consequently, we may not be able to utilize a material portion of our NOLs and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Changes in tax law may adversely affect us or our investors.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. For example, under Section 174 of the Code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the U.S. will be capitalized and amortized, which may have an adverse effect on our cash flow. In recent years, many such changes have been made, and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

A portion of our chemistry-based product development and sourcing of certain manufacturing raw materials for our product candidates takes place outside the United States through third-party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest in China could materially adversely affect our business, financial condition and results of operations.

We currently contract certain product development and manufacturing operations to third parties outside the United States, including in China, and we expect to continue to use such third-party manufacturers for such product candidates. Any disruption in production or inability of our manufacturers outside the United States to produce adequate quantities to meet our needs, whether as a result of a natural disaster or other causes, could impair our ability to operate our business on a day-to-day basis and to continue our development of our product candidates. Furthermore, since these manufacturers are located outside the United States, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or other foreign governments, political unrest or unstable economic conditions in these jurisdictions. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China. Any of these matters could materially adversely affect our business, financial condition and results of operations. Any recall of the manufacturing lots or similar action regarding our product candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third-party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to foreign currency fluctuations in the value of the local currency as future appreciation of the local currency could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to

increased demand for skilled laborers and the availability of skilled labor declines outside the United States, including in China.

Risks Related to Reliance on Third Parties

We currently rely, and plan to rely in the future, on third parties to conduct and support our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.

We have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs, and strategic partners to conduct and support our preclinical studies and clinical trials under agreements with us. We are continuing to build our internal chemistry, manufacturing and controls, biology and preclinical development capabilities to supplement activities conducted by third parties on our behalf. As part of this personnel build out, we may incur additional costs or experience delays in engaging directly with other third-party CROs and CMOs.

We expect to have to negotiate budgets and contracts with CROs, trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

We will rely heavily on these third parties over the course of our preclinical studies and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with pharmaceutical product produced under cGMP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our preclinical studies or clinical trials will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our product candidates. These third parties may also have relationships with other commercial entities, including

our competitors, for whom they may also be conducting preclinical studies, clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our preclinical or clinical protocols or regulatory requirements or for other reasons, our preclinical studies or clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be adversely affected, our costs could increase and our ability to generate revenue could be delayed.

Switching or adding third parties to conduct our preclinical studies and clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines.

We currently rely and expect to rely in the future on the use of dedicated manufacturing suites in third-party facilities or on third parties general manufacturing facilities to manufacture our product candidates, and we may rely on third parties to develop processes and testing methods for our products, if approved. Our business could be adversely affected if we are unable to use third-party manufacturing suites or if the third-party manufacturers fail to develop appropriate processes and testing methods to provide us with sufficient quantities of our product candidates or fail to do so at acceptable quality levels or prices.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must currently rely on outside vendors to manufacture our product candidates. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our product candidates, if approved. We will need to negotiate and maintain contractual arrangements with these outside vendors for the supply of our product candidates and we may not be able to do so on favorable terms.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other comparable foreign regulatory authorities following inspections that will be conducted after we submit an application to the FDA or other comparable foreign regulatory authorities. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or other regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance, qualified personnel, their equipment and facilities and any applicable licenses or approvals. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs and delays, and materially adversely affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, if any third-party manufacturers on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected.

Our anticipated reliance on a limited number of third-party manufacturers exposes us to a number of risks, including the following:

- we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA or other comparable foreign regulatory authority must inspect any manufacturers for cGMP compliance as part of our marketing application;
- manufacturing processes and testing methods will need to be transferred to a new manufacturer, or develop substantially equivalent processes and testing methods for, the production of our product candidates;
- our third-party manufacturers might be unable to timely manufacture our product candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any;
- contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our future contract manufacturers may not perform as agreed, may not devote sufficient resources to our product candidates or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products, if any;

- contract manufacturers are subject to ongoing periodic unannounced inspection by the FDA or other comparable foreign regulatory authority and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards and we have no control over third-party manufacturers' compliance with these changing and tightening regulations and standards;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates;
- our third-party manufacturers could breach or terminate their agreements with us;
- our third-party manufacturers may experience change of control of their ownership including ownership by a competitor,
- raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available at acceptable prices, or at all, or may not be suitable or acceptable for use due to material or component defects;
- our contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man-made disasters; and
- our contract manufacturers may have unacceptable or inconsistent product quality success rates and yields, and we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance, qualified personnel, their equipment and facilities and any applicable licenses or approvals.

Our business could be materially adversely affected by business disruptions to our third-party providers that could materially adversely affect our potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the initiation or completion of any clinical trials or the approval of any of our product candidates by the FDA or other comparable foreign regulatory authority, result in higher costs or adversely impact commercialization of our product candidates. In addition, we will rely on third parties to perform certain specification tests on our product candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm and the FDA or other comparable foreign regulatory authority could place significant restrictions on our company until deficiencies are remedied.

We currently, and may in the future, depend on single-source suppliers for some of the ingredients, components and materials used in, and the manufacturing processes required to develop, our product candidates.

We currently, and may in the future, depend on single-source suppliers for some of the ingredients, raw materials, components and materials used in, and development activities required to manufacture our product candidates. There are, for certain of these components, relatively few alternative sources of supply and there is limited need for multiple suppliers at this stage of our business. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs, be able to supply materials or services to us at cost that are acceptable to us, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, ingredients, components, key processes and finished goods exposes us to several risks, including disruptions in supply, price increases or late deliveries. These suppliers may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single-source supplier or service provider could lead to supply delays or interruptions which would materially adversely affect our business, financial condition and results of operations.

If we have to switch to a replacement supplier, the manufacture and delivery of our product candidates may be interrupted for an extended period, which could materially adversely affect our business. Establishing additional or replacement suppliers for any of the components or processes used in or for our product candidates, if required, may not be accomplished quickly and would create increased cost, or adversely impact the quality of our product candidates. If we are able to find a replacement supplier, the replacement supplier would need to be qualified, would need to process our technology transfer and may require additional regulatory authority approval, which could result in further delay. While we seek to maintain adequate inventory of the single-source ingredients, components and materials used in our product candidates, any interruption or delay in the supply of ingredients, components or materials or our inability to obtain ingredients, components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our product candidates.

If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. Our manufacturers may use highly flammable reagents at high reaction temperature, are subject to federal, state and local laws and regulations in the United States and their country governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards and regulations, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

We may, in the future, form or seek collaborations or strategic alliances or enter into licensing arrangements, and we may not realize the benefits of such collaborations, alliances or licensing arrangements.

We may, in the future, form or seek strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy and obtain marketing approval.

Further, collaborations involving our product candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaborators may own or co-own intellectual property covering our product candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into future collaboration agreements and strategic partnerships or license our product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Furthermore, if conflicts arise between our future corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Any delays in entering into future collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and/or acquire intangible assets that could result in significant future amortization expense.

Risks Related to Intellectual Property

If we are unable to obtain, maintain, enforce and adequately protect our patents and other intellectual property rights with respect to our technology and product candidates, or if the scope of our patents or other intellectual property rights are not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology or product candidates may be adversely affected.

We rely on a combination of patent applications, trade secret protection and confidentiality agreements to protect the intellectual property related to our technology and product candidates, and our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to such technology and product candidates. We will only be able to protect our product candidates, proprietary technologies and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or trade secret protections cover them. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal, factual and scientific questions and can be uncertain. In recent years, patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent

applications may not result in patents being issued in the United States or in other jurisdictions which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products.

The patent applications that we own may fail to result in issued patents with claims that cover our technology or product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our technology or product candidates, third parties may challenge the inventorship, ownership, validity, enforceability or scope of such patents, which may result in such patents being narrowed or invalidated, or being held unenforceable. Our pending and future patent applications may not issue to protect our technology or product candidates or which effectively prevent others from developing, manufacturing or commercializing competitive technologies and product candidates. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. This will require us to be cognizant of the time from invention to filing of a patent application, and beyond.

If the breadth or strength of protection provided or potentially provided by the patents and patent applications we hold with respect to our technology or product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Furthermore, even if our patents and patent applications are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our technology and product candidates or prevent others from designing around our claims. In addition, no assurances can be given that third parties will not create similar or alternative technologies, products or methods that achieve similar results without infringing upon our patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity or enforceability, and our patents may be challenged in courts or patent offices in the United States and abroad. In addition, the issuance of a patent does not give us the right to practice the patented invention, as third parties may have blocking patents that could prevent us from marketing our product candidate, if approved, or practicing our own patented technology.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, we may become involved in litigation, opposition, interference, derivation, post grant review, *inter partes* review or other proceedings challenging our patent rights, and the outcome of any proceedings are highly uncertain. Such challenges may result in the patent claims of our owned or in-licensed patents being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage.

If any of our patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and further, may infringe our patents in territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

However, trade secrets can be difficult to protect and trade secret protection will not protect us from innovations that a competitor develops independently of our proprietary know how. If a competitor independently develops a technology that we protect as a trade secret and files a patent application on that technology, then we may not be able to patent that technology in the future, may require a license from the competitor to use our own know-how, and even then, the license may not be available on commercially-reasonable terms. Further, we cannot provide any assurances that competitors or other third parties will not otherwise gain access to our trade secrets and other confidential proprietary information or independently discover or develop substantially equivalent technology and processes. If we are unable to prevent disclosure of the trade secrets and other non-patented intellectual property related to our product candidates and technologies to third parties, there is no guarantee that we will have any such enforceable trade secret protection and we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with parties who have access to them, such as our employees, consultants, scientific advisors and other contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and our trade secrets could be disclosed, and we may not have adequate remedies for any such breach.

Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, and this scenario could materially adversely affect our business, financial condition and results of operations.

Our success depends in part on our ability to protect our intellectual property rights. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to protect our intellectual property rights throughout the world.

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and product candidates and any future products. These candidates include BMF-219 and others, their respective components, formulations, methods used to manufacture them and methods of treatment. Our commercial success will also depend on successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our technology, product and product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our pending and future patent applications may not result in issued patents that protect our technology or products, in whole or in part. In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies.

If we delay in filing a patent application, and a competitor files a patent application on the same or a similar technology before we do, we may face a limited ability to secure patent rights or we may not be able to patent the technology at all. Even if we can patent the technology, we may be able to patent only a limited scope of the technology, and the limited scope may be inadequate to protect our products, or to block competitor products that are similar or adjacent to ours. Our earliest patent filings have been published. A competitor may review our published patents and arrive at the same or similar technology advances for our products as we developed.

If the competitor files a patent application on such an advance before we do, then we may no longer be able to protect the technology or product, we may require a license from the competitor, and if then the license may not be available on commercially-reasonable terms.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we fail to comply with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Any issued patents we may own covering our product candidates could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad, including the USPTO.

Any of our intellectual property rights could be challenged or invalidated despite measures we take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary technology. For example, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the U.S. and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material information from the USPTO or the applicable foreign counterpart, or made a misleading statement, during prosecution. A litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such a challenge is unpredictable.

With respect to challenges to the validity of our patents, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. The cost of defending such a challenge, particularly in a foreign jurisdiction, and any resulting loss of patent protection could have a material adverse impact on one or more of our product candidates and our business. Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend, particularly in a foreign jurisdiction, and could require us to pay substantial damages, cease the sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially-reasonable terms or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel.

We may become involved in lawsuits or litigation at the USPTO to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors and other third parties may infringe or otherwise violate our or our future licensor's patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file infringement, misappropriation or other intellectual property-related claims against such parties, which can be expensive and time consuming. To counter infringement or other unauthorized use, we may be required to file claims on a country-by-country basis, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such claims, which often last for years before they are concluded. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question.

In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or those of our future licensors is threatened, it could dissuade other companies from collaborating with us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Even if we establish infringement, misappropriation or other violation of our intellectual property, the court may decide not to grant an injunction against further such activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings.

We may be required to protect our patents through procedures created to attack the validity of a patent at the USPTO. The USPTO hears post-grant proceedings, including post grant review (PGR), *inter partes* review (IPR), and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product or product candidate, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized as products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours for a meaningful amount of time, or at all.

Depending upon the timing, duration and conditions of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union and certain other countries. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. Only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14

years from approval, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for the applicable product candidate will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be expected, and our competitive position, business, financial condition, results of operations and prospects could be materially adversely affected.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate. Any of the foregoing could adversely affect our competitive position, business, financial condition, results of operations and prospects.

Changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our technology, products and product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our or future licensor's patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. United States Congress has in recent years considered legislation to reduce the term of certain drug patents in order to ease generic entry and increase competition. Evolving judicial interpretation of patent law could also adversely affect our business. For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our technology or product candidates. Also, former employees may become employed by competitors who develop similar technology or product candidates, and could assist the competitor in designing around our patents or trade secrets. While it is our policy to require our employees and contractors who may be involved in the development of our intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or our ownership of our patents, trade secrets or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our technology or product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We use and will continue to use registered and/or unregistered trademarks or trade names to brand and market ourselves and any products that we develop. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain. Defending against such lawsuits will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our technology, product candidates and products and use our proprietary technologies without infringing the proprietary rights of third parties. U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields relating to our technology, product candidates and products. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our technology, product candidates or products infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our technology, product candidates and products.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our issued patents or our pending applications, or that we were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our patent applications or patents, which could require us to obtain rights to issued patents covering such technologies.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our technology, product candidates and/or products infringe or misappropriate their intellectual property rights.

If a third party claims that we infringe or misappropriate its intellectual property rights, we may face a number of issues, including, but not limited to: infringement, misappropriation and other intellectual property related claims, which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business; substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement or misappropriation was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees; a court prohibiting us from developing, manufacturing, marketing or selling our products or product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us; however, the third party is not required to grant the license; if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products; and redesigning our technology, product candidates or products so they do not infringe such third party patents; redesign may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any

litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in *ex-parte* re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office (EPO), or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO, or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our technology, product candidates or products.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common stock to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or alleged trade secrets of third parties or competitors or are in breach of non-competition or non-solicitation agreements with our competitors or their former employers.

As is common in the biotechnology and pharmaceutical industries, we employ individuals and engage the services of consultants who previously worked for other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that our consultants have used or disclosed trade secrets or other proprietary information of their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

If we fail to comply with our obligations in any future agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with any licensors, we could lose license rights that are important to our business.

The growth of our business may depend in part on our ability to acquire or in-license additional proprietary rights from third parties in the future. For example, our programs may involve additional product candidates that may require the use of proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compounds and pre-existing pharmaceutical compounds. These pharmaceutical compounds may be covered by intellectual property rights held by others. Thus, we may in the future enter into license agreements with third parties under which we receive rights to intellectual property that are important to our business. These intellectual property license agreements may impose on us various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to bankruptcy-related proceedings, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

We may also in the future enter into license agreements with third parties under which we are a sublicensee. If our sublicensor fails to comply with its obligations under its upstream license agreement with its licensor, the licensor may have the right to terminate the upstream license, which may terminate our sublicense. If this were to occur, we would no longer have rights to the applicable intellectual property unless we are able to secure our own direct license with the owner of the relevant rights, which we may not be able to do on reasonable terms, or at all, which may impact our ability to continue to develop and commercialize our product candidates incorporating the relevant intellectual property.

We may need to obtain licenses in the future from third parties to advance our research or allow commercialization of our technology, product candidates or products, and we cannot provide any assurances that there are no third-party patents which might be enforced against our technology, product candidates or products in the absence of such a license. We may fail to obtain any of these licenses on commercially-reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected technology, product candidates or products, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property from third parties may become of critical importance to our business, which involves complex legal, business and scientific issues. Disputes may arise between us and our future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we license in the future prevent or impair our ability to maintain our licensing arrangements on commercially-reasonable terms, we may not be able to successfully develop and commercialize the affected technology, product candidates or products, which would have a material adverse effect on our business.

In addition, certain of our future agreements with third parties may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, we may in the future enter into license agreements that are not assignable or transferable, or that require the licensor's express consent in order for an assignment or transfer to take place.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make product candidates that are similar to ours but that are not covered by the claims of the patents that we own;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or in-licensed intellectual property rights;

- it is possible that our owned and in-licensed pending patent applications or those we may own or in-license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;
- we may not develop additional proprietary technologies that are patentable;
- the patents or intellectual property rights of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Common Stock

The price of our stock has been and is likely to continue to be volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

The trading price of our common stock has been and is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section and elsewhere herein, these factors include:

- the timing, progress, costs and results of our ongoing, planned or any future preclinical studies, clinical trials or clinical development programs;
- the commencement, enrollment, progress or results of clinical trials of our product candidates or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results or delays in preclinical studies and clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial, including due to the suspension of a clinical trial by the FDA or other regulatory authorities;
- any delay in our regulatory filings or any adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- changes in laws or regulations applicable to our product candidates and any future products, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers or our manufacturing plans;
- our inability to obtain adequate product supply for any licensed product or inability to do so at acceptable prices;
- our inability to establish collaborations if needed;
- our failure to commercialize our product candidates;
- additions or departures of key scientific or management personnel;

- unanticipated serious safety concerns related to the use of our product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- the size and growth of our initial cancer target markets;
- our ability to successfully treat additional types of cancers or at different stages;
- our ability to develop our product candidates for the treatment of type 2 diabetes or other metabolic diseases;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or menin inhibitors in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- changes in the structure of healthcare payment systems;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to intellectual property or proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including intellectual property or stockholder litigation;
- the impact of any natural disasters or public health emergencies, such as the ongoing COVID-19 pandemic;
- inflationary pressures and general economic, political, industry and market conditions; and
- other events or factors, many of which are beyond our control.

The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In particular, the trading prices for pharmaceutical, biopharmaceutical and biotechnology companies have been highly volatile as a result of the ongoing COVID-19 pandemic. In addition, broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. If the market price of our common stock does not exceed the initial public offering price, you may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would materially adversely affect our business, financial condition and results of operation.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation preferences or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships, alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. A significant portion of our outstanding shares of common stock are held by a small number of stockholders, including our directors, officers and significant stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

We have also registered or intend to register all shares of our common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. As a result, these shares will be available for sale in the public market subject to vesting arrangements and exercise of options, and restrictions under applicable securities laws. In addition, our directors, executive officers and certain affiliates have established or may in the future establish programmed selling plans under Rule 10b5-1 of the Exchange Act for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, would result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. In October 2022, we filed a registration statement on Form S-3 relating to the registration of our common stock, preferred stock, debt securities, warrants and units or any combination thereof. In November 2022, we entered into an "at-the-market" offering program, or ATM, which provides for the offering, issuance and sale by us of shares of our common stock from time to time for aggregate gross proceeds of up to $100 million in sales deemed to be "at-the-market offerings" as defined by the Securities Act of 1933, as amended. We have not yet sold or issued any shares of common stock pursuant to the ATM. Any sale or issuance of securities pursuant to this registration statement or otherwise may result in dilution to our stockholders and may cause the market price of our stock to decline. Furthermore, new investors purchasing securities that we may issue and sell in the future could obtain rights superior to the rights of our existing stockholders.

We are also authorized to grant stock options and other equity-based awards to our employees, directors and consultants pursuant to our 2021 Incentive Award Plan, or Incentive Plan. The number of shares available for future grant under the Incentive Plan will automatically increase each year on January 1, from January 1, 2022 to January 1, 2031, by the lesser of (A) five percent of the shares of Common Stock outstanding on the last day of the immediately preceding fiscal year and (B) such smaller number of shares as determined by the Board or the Committee (as defined in the Incentive Plan). We have also reserved shares of common stock for issuance pursuant to our 2021 Employee Stock Purchase Plan, or ESPP, which number of shares will automatically increase each year on January 1, from January 1, 2022 to January 1, 2031, by the lesser of (i) one percent of the shares of Common Stock outstanding on the last day of the immediately preceding fiscal year and (ii) such number of shares as may be determined by the Board (as defined in the ESPP); provided, however, no more than 4,500,000 shares may be issued under the ESPP. Currently, we plan to register any increase in the number of shares available for issuance under the Incentive Plan and the ESPP promptly following the effectiveness of any such increase. If our board of directors elects to increase the number of shares available for future grant under the Incentive Plan or the ESPP, our stockholders may experience additional dilution, and our stock price may fall.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.

Our executive officers, directors and their respective affiliates beneficially own approximately 29% of our outstanding voting stock as of December 31, 2022. In particular, Thomas Butler and Ramses Erdtmann are executive officers and directors and are affiliates of Point Sur Investors Fund I, LP and Point Sur Investors LLC, and Bihua Chen is a director and an affiliate of the entities affiliated with Cormorant Asset Management. These stockholders, acting together, may be able to impact matters requiring stockholder approval. For example, they may be able to impact elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

We do not intend to pay dividends on our capital stock, so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our capital stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which other terms prohibiting or limiting the amount of dividends that may be declared or paid on our capital stock. Any return to stockholders will therefore be limited to any appreciation in the value of their stock.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. These provisions, among other things:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan (poison pill);
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting;
- authorize our board of directors to amend the bylaws;
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and
- require a super-majority vote of stockholders to amend some provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL) prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a

premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws provide for an exclusive forum in the Court of Chancery of the State of Delaware for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware (or, in the event that the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause or causes of action against any defendant arising under the Securities Act. Such provision is intended to benefit and may be enforced by us, our officers and directors, employees and agents, including the underwriters and any other professional or entity who has prepared or certified any part of this report. Nothing in our amended and restated certificate of incorporation or amended and restated bylaws precludes stockholders that assert claims under the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

We believe these provisions may benefit us by providing increased consistency in the application of Delaware law and federal securities laws by chancellors and judges, as applicable, particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims or make such lawsuits more costly for stockholders, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive-forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. If a court were to find the choice of forum provision that will be contained in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the DGCL, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;

- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;
- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

While we maintain a directors' and officers' insurance policy, such insurance may not be adequate to cover all liabilities that we may incur, which may reduce our available funds to satisfy third-party claims and may materially adversely affect our cash position.

General Risk Factors

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could materially adversely affect our business.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including, our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our current product candidates and any future product candidates and research-stage programs, which will change from time to time;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the cost of manufacturing our current product candidates and any future product candidates, which may vary depending on FDA or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies or other assets;
- the timing and outcomes of clinical trials for our current and future product candidates, or competing product candidates;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;

- competition from existing and potential future products that compete with our product candidates and any of our future product candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval of our product candidates;
- the level of demand for our future product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future products that compete with our product candidates;
- our ability to commercialize our product candidates, if approved, inside and outside of the United States, either independently or working with third parties;
- our ability to establish and maintain future collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic and political environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

We will continue to incur significant costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (Exchange Act), which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, under the Dodd-Frank Wall Street Reform and Consumer Protection Act (Dodd-Frank Act), the SEC has adopted significant corporate governance and executive compensation related rules and regulations, such as “say on pay” and proxy access. While emerging growth companies are permitted to implement many of these requirements over a longer period and up to five years from the pricing of the IPO, we cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of any products that we develop, if approved. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

As a result of being a public company, we are obligated to develop and maintain proper and effective controls over financial reporting. If we fail to maintain proper and effective internal controls over financial reporting in the future, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to Section 404 of Sarbanes-Oxley Act, our management is required to report upon the effectiveness of our internal controls over financial reporting. When we lose our status as an "emerging growth company," as defined in the JOBS Act, and reach an accelerated filer threshold, our independent registered public accounting firm will be required to attest to the effectiveness of our internal controls over financial reporting. However, for so long as we remain an emerging growth company, we intend to take advantage of an exemption available to emerging growth companies from these auditor attestation requirements. The rules governing the standards that must be met for management to assess our internal controls over financial reporting are complex and require significant documentation, testing, and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we will need to upgrade our systems including information technology; implement additional financial and management controls, reporting systems, and procedures; and hire additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal controls over financial reporting is effective, investors may lose confidence in our financial reporting, and the trading price of our common stock may decline.

We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal controls over financial reporting in the future. Any failure to maintain internal controls over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal controls over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal controls over financial reporting once that firm begins its Section 404 reviews, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Global Select Market, the SEC, or other regulatory authorities. Failure to remedy any material weakness or significant deficiencies in our internal controls over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act the regulations of the Nasdaq Global Select Market, the rules and regulations of the SEC, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal controls over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. Commencing with our fiscal year ending on December 31, 2022, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act and we may experience difficulty in meeting these reporting requirements in a timely manner.

We expect that we will need to hire additional accounting, finance, and other personnel in connection with our efforts to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements which may result in substantial costs. Any disruptions or difficulties in implementing or using our finance and accounting systems could adversely affect our controls and harm our business. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention. In addition, we may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be

harmed, investors could lose confidence in our reported financial information and we could be subject to sanctions or investigations by the Nasdaq Global Select Market, the SEC or other regulatory authorities.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the facts that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Future changes in financial accounting standards or practices may cause adverse and unexpected revenue fluctuations and adversely affect our reported results of operations.

Future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our reported financial position or results of operations. Financial accounting standards in the United States are constantly under review and new pronouncements and varying interpretations of pronouncements have occurred with frequency in the past and are expected to occur again in the future. As a result, we may be required to make changes in our accounting policies. Those changes could affect our financial condition and results of operations or the way in which such financial condition and results of operations are reported. We intend to invest resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from business activities to compliance activities. For additional information, see the section of this Annual Report on Form 10-K titled "Financial Statements and Supplementary Data—Notes to Financial Statements—Recent Accounting Pronouncements."

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company and, for as long as we continue to be an emerging growth company, we intend to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements; and
- exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, our financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.235 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than $1 billion in non-convertible debt securities during the prior three-year period; and (iv) December 31, 2026.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including

not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use, or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations, or ordinances could be interpreted, changed, modified, or applied adversely to us. For example, the Tax Act enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

The global credit and financial markets have recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, uncertainty about economic stability and changes in fiscal policy, including higher interest rates. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget.

If our security measures are compromised, or the security, confidentiality, integrity, or availability of our information technology, software, services, communications or data is compromised, limited or fails, this could result in a material adverse impact.

If we or third parties related to us (such as our partners, CROs, and CMOs) have experienced or in the future experience any security incidents that result in any deletion or destruction of, unauthorized access to, loss of, unauthorized acquisition or disclosure of, or inadvertent exposure disclosure of, sensitive, confidential, or proprietary information (Sensitive Information), or a compromise related to the security, confidentiality, integrity or availability of our (or their) information technology, software, services, communications, or data, it may result in a material adverse impact, including without limitation, regulatory investigations or enforcement actions, litigation, indemnity obligations, delays to the development and commercialization of our product candidates, disruption of our programs, negative publicity, and financial loss. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the ongoing COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We or third parties related to us may also experience security breaches that may remain undetected for an extended period. Further, we have outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. If our third-party vendors fail to protect their information technology systems and our confidential and proprietary information, we may also be vulnerable to disruptions in service and unauthorized access to our confidential or proprietary information.

Further, systems containing Sensitive Information are vulnerable to service interruptions, malfunction, natural disasters, terrorism, war, software and hardware failures, telecommunication and electrical failures, theft or loss from inadvertent or intentional actions by employees, contractors, consultants, business partners and/or other third parties, malware, malicious code (such as viruses and worms), software bugs, ransomware, denial-of-service attacks (including credential stuffing), social engineering and other means that affect service reliability and threaten the security, confidentiality, integrity and availability of information).

We cannot assure you that our security efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties related to us, will prevent breakdowns or breaches in systems or other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage to, Sensitive Information that could have a material adverse impact. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation and/or unauthorized access, use or disclosure of, or the prevention of access to, data (including trade secrets or other confidential information, intellectual property, proprietary business information and personal information), which could result in a material adverse impact including financial, legal, business and reputational harm. For example, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under privacy, data protection, and information security laws and regulations, which could result in significant legal and financial exposure and reputational damages that could potentially have a material adverse impact.

Notifications and follow-up actions related to a security incident could impact our reputation and cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse impact. To the extent that any disruption or security incident were to result in a loss, destruction or alteration of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with applicable privacy, data protection, and information security laws and regulations.

Our insurance policies, if any, may not be adequate to compensate us for the potential losses arising from any such security incident. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations may involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations may also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

If securities or industry analysts do not publish research or reports, or if they publish adverse or misleading research or reports, regarding us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. We do not currently have and may never obtain research coverage by securities or industry analysts. If no or few securities or industry analysts commence coverage of us, the stock price would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our business could be negatively impacted by corporate citizenship and environmental, social and corporate governance matters and/or our reporting of such matters.

There is an increasing focus from certain investors, consumers, and other stakeholders concerning corporate citizenship and sustainability matters. We could be perceived as not acting responsibly in connection with these matters. Our business could be negatively impacted by such matters. Any such matters, or related corporate citizenship and sustainability matters, could have a material adverse effect on our business.

Geopolitical risks associated with the ongoing military conflict between Russia and Ukraine could have an adverse impact on our business, financial condition and results of operations, including our clinical trials.

In late February 2022, Russia commenced a military invasion of Ukraine, and sustained conflict and disruption in the region is likely. The uncertain nature, magnitude, and duration of hostilities stemming from the conflict in Ukraine, including the potential effects of sanctions limitations, retaliatory cyber-attacks on the world economy and markets, have contributed to increased market volatility and uncertainty, which could have an adverse impact on macroeconomic factors that affect our business and operations.

Sanctions imposed by the United States, European Union, and other countries in response to the conflict between Russia and Ukraine and the potential response to such sanctions may have an adverse impact our business, including our clinical trials, the financial markets and the global economy. As the conflict in Ukraine continues, there can be no certainty regarding whether such governments or other governments will impose additional sanctions, or other economic or military measures relating to Russia, which could further adversely affect market and economic conditions.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We currently lease approximately 45,799 square feet of office, laboratory and manufacturing space in Redwood City and San Carlos, California under three leases which expire in July 2025 and January 2027. We believe these facilities are sufficient to meet our near-term needs and that any additional space we may require will be available on commercially reasonable terms.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently a party to any material legal proceedings. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity, reputational harm and other factors.

Item 4. Mine Safety Disclosures

Not Applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information for Our Common Stock

Our common stock has been listed on the Nasdaq Global Select Market under the symbol "BMEA" since April 16, 2021. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of March 21, 2023, there were 46 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid cash dividends on our capital stock to investors. We currently intend to retain all available funds and any future earnings to support operations and to finance the growth and development of our business. We do not intend to declare or pay any cash dividends on our capital stock in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors, subject to applicable laws, and will depend upon, among other factors, our results of operations, financial condition, contractual restrictions and capital requirements. Our future ability to pay cash dividends on our capital stock may be limited by the terms of any future debt or preferred securities.

Unregistered Sales of Equity Securities

Since January 1, 2020, the Company has not issued any unregistered securities except as disclosed in Part II, Item 15 of Amendment No. 2 to the Company's Registration Statement on Form S-1 filed on April 15, 2021.

Use of Proceeds from Registered Securities

On April 15, 2021, our registration statement on Form S-1 (File No. 333-254793), was declared effective in connection with our IPO. There has been no material change in the planned use of proceeds from our IPO as described in the registration statement on Form S-1.

Purchases of Equity Securities by Issuers and Affiliated Purchasers

None.

Item 6. Selected Financial Data

Not Applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described, in or implied, by these forward-looking statements.

We were established in the state of Delaware in August 2017 as Biomea Fusion, LLC. In December 2020, all outstanding membership interests in Biomea Fusion, LLC were converted into equity interests in Biomea Fusion, Inc. The capitalization information included in this Annual Report on Form 10-K is consistently presented as the information of Biomea Fusion, Inc., even during the prior period when our stockholders held their equity interests in Biomea Fusion, LLC.

Overview

We are a clinical-stage biopharmaceutical company 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 an orally bioavailable, potent and selective covalent inhibitor of menin, built from our FUSION System. We currently have clinical studies of BMF-219 underway in patients with liquid and solid tumors, as well as patients with type 2 diabetes. Menin is an important transcriptional regulator known to play a direct role in oncogenic signaling in multiple cancers and in beta cell homeostasis. Menin also serves as a checkpoint to prevent beta cell proliferation. Thus, we believe inhibiting menin via BMF-219 has the potential to enable the proliferation, preservation, and reactivation of healthy, function beta cells capable of producing insulin, thereby leading to long-term glycemic control in patients with type 2 diabetes.

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, normalizing glucose levels during treatment and even after drug washout. As of December 31, 2022, BMF-219 is being evaluated in up to eight liquid and solid tumor types and in type 2 diabetes across three 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. In May 2022, we announced the nomination of our second development candidate, BMF-500, a covalent inhibitor of FLT3, and presented preclinical data on this program in December 2022. We expect to file an Investigational New Drug application (IND) with the U.S. Food and Drug Administration (FDA) to study BMF-500 in acute leukemias in the first half of 2023.

We are currently advancing additional preclinical covalent programs for the treatment of select diseases and expect to nominate our third development candidate in the first half of 2023. Our goal is to utilize our capabilities and FUSION System platform to become the leader in developing covalent small molecules to maximize the depth and durability of clinical benefit when treating various diseases.

Since commencing operations in 2017, we have devoted substantially all of our efforts and financial resources to conducting research and development activities, including drug discovery and preclinical studies, establishing and maintaining our intellectual property portfolio, the manufacturing of clinical and research material, organizing and staffing our company, business planning, raising capital and providing general and administrative support for these operations. We have not generated any revenue from product sales and, as a result, we have never been profitable and have incurred net losses since commencement of our operations.

As of December 31, 2022, we had an accumulated deficit of $131.6 million. We incurred net losses of $81.8 million and $41.6 million for the years ended December 31, 2022 and 2021, respectively. Based on our current operating plan, we believe that our existing cash and cash equivalents, restricted cash, and investments as of December 31, 2022, without any future financing, will not be sufficient for the Company to continue as a going concern for at least one year from the issuance date of the financial statements appearing elsewhere in this Annual Report on Form 10-K. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, and our net losses may fluctuate significantly from period to period, depending on the timing of and expenditures on our planned research and development activities.

We do not expect to generate revenue from product sales unless and until we obtain regulatory approval for and commercialize a product candidate, and we cannot assure you that we will ever generate significant revenue or profits. We expect that our expenses will continue to increase for the foreseeable future. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- continue our research and development efforts and submit additional INDs;
- conduct our ongoing preclinical studies and Phase 1 clinical trial of BMF-219 in various types of liquid tumors, our planned Phase 1/1b clinical trial of BMF-219 in solid tumors with KRAS mutations, and our Phase 1/2 clinical trial of BMF-219 in type 2 diabetes;

- conduct preclinical studies and initiate and conduct clinical trials;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges;
- establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities, whether alone or with third parties, to commercialize any product candidates for which we may obtain regulatory approval, if any;
- obtain, expand, maintain, enforce and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel; and
- operate as a public company.

We may need to raise additional capital in the future to fund our operations, including to conduct and complete clinical trials for any product candidates. If sufficient funds on acceptable terms are not available when needed, we could be required to significantly reduce our operating expenses and delay, reduce the scope of, or eliminate one or more of our development programs.

We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates. All of our product candidates are small molecules and are manufactured in synthetic processes from available or custom synthesized starting materials. The chemistry is scalable and uses commonly available pharmaceutical equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities. In addition, we do not yet have a marketing or sales organization or commercial infrastructure. Accordingly, we will incur significant expenses to develop a marketing and sales organization and commercial infrastructure in advance of generating any product sales.

In April 2021, we completed our initial public offering (IPO) and issued an aggregate of 9,000,000 shares of our common stock at a price of $17.00 per share. Subsequent to the close, an additional 823,532 shares were issued in connection with the partial exercise by the underwriters of their option to purchase additional shares of common stock. In addition, immediately prior to the closing of the IPO, all outstanding shares of our convertible preferred stock automatically converted into 7,064,925 shares of common stock. Proceeds from the IPO, net of underwriting discounts and commissions and offering costs were $152.8 million.

The global COVID-19 pandemic continues to evolve rapidly, and we will continue to monitor it closely. The extent of the impact of the ongoing COVID-19 pandemic on our business, operations, and product development timelines and plans remains uncertain and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, trial sites, contract research organizations (CROs), contract manufacturing organizations (CMOs), and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. We have not experienced delays in our discovery and development activities as a result of the ongoing COVID-19 pandemic, but may in the future as some of our CROs and other service providers continue to be impacted.

Components of Operating Results

Revenue

To date, we have not generated any revenue and do not expect to generate any revenue from the sale of products in the near future.

Operating Expenses

Research and Development

Our research and development expenses consist primarily of external and internal costs incurred in connection with the research and development of our research programs and product candidates.

External costs include:

- expenses incurred under agreements with third-party CMOs, CROs, research and development service providers, academic research institutions and consulting costs; and
- laboratory expenses, including supplies and services.

Internal costs include:

- personnel-related expenses, including salaries, benefits and stock-based compensation for personnel in research and product development roles; and
- facilities and other allocated expenses, including expenses for rent and facilities maintenance, and depreciation.

We expense research and development costs in the periods in which they are incurred. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and as services are performed. We track direct costs by stage of program, clinical or preclinical. However, we do not track indirect costs on a program specific or stage of program basis because these costs are deployed across multiple programs and, as such, are not separately classified.

We expect our research and development expenses to increase substantially during the next few years as we seek to initiate and complete clinical trials, pursue regulatory approval of BMF-219, and advance other programs, including BMF-500, through preclinical and clinical development. Predicting the timing or the final cost to complete our clinical program or validation of our manufacturing and supply processes is difficult and delays may occur because of many factors. The process of conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and time-consuming. To the extent that our product candidates continue to advance into clinical trials, as well as advance into larger and later stage clinical trials, our expenses will increase substantially and may become more variable.

Our future research and development costs may vary significantly based on a wide variety of factors, such as:

- the scope, rate of progress, expense and results of our ongoing preclinical development activities and Phase 1 clinical trial of BMF-219 in various types of cancer, as well as of any future preclinical development and clinical trials of our product candidates, including BMF-500, and other research and development activities we may conduct, such as our Phase 1/2 clinical trial of BMF-219 in type 2 diabetes;
- uncertainties in clinical trial design and the interpretation of clinical trial data;
- per patient trial costs;
- the duration, scope and number of trials required for approval;
- the number of sites included in the trials;
- the number of patients who participate in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the drop-out or discontinuation rates of patients, particularly in light of the ongoing COVID-19 pandemic environment;
- the safety and efficacy profiles of our product candidates;
- the timing receipt, and terms of any approvals from applicable regulatory authorities including the FDA and non-U.S. regulators;
- maintaining a continued acceptable safety profile of our product candidates following approval, if any, of any of our product candidates;
- significant and changing government regulation and regulatory guidance;
- establishing clinical and commercial manufacturing capabilities or making arrangements with third-party manufacturers in order to ensure that we or our third-party manufacturers are able to make product successfully;
- the impact of any business interruptions to our operations or to those of the third parties with whom we work, particularly considering the ongoing COVID-19 pandemic environment and adverse global market conditions; and
- the extent to which we establish additional strategic collaborations or other arrangements.

A change in the outcome of any of these variables with respect to the development of any or our product candidates could significantly change the costs and timing associated with the development of that product candidate. The actual probability of success for our product candidates may be affected by a variety of factors, including the safety and efficacy of our product candidates, investment in our clinical programs, manufacturing capability and competition with other products and product candidates. As a result of these variables, we are unable to determine the duration and completion costs of our research and

development projects or when and to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in achieving regulatory approval for any of our product candidates.

General and Administrative

General and administrative expenses consist principally of personnel-related costs including payroll and stock-based compensation expense for personnel in executive, finance, human resources, business and corporate development, and other administrative functions, professional fees for legal, consulting, and accounting services, rent and other facilities costs, depreciation, and other general operating expenses not otherwise classified as research and development expenses.

We anticipate that our general and administrative expenses will increase substantially during the next few years as a result of staff expansion and additional occupancy costs, as well as costs associated with being a public company, including compliance with the rules and regulations of the SEC and those of any national securities exchange on which our securities are traded, higher legal and auditing fees, investor relations costs, higher insurance premiums and other compliance costs associated with being a public company. We also expect that our future intellectual property expenses may increase as we expand our product portfolio of product candidates due to advances in our research and development programs.

Interest and Other Income, Net

Interest and other income, net consists primarily of interest earned on our investments and non-cash interest income (loss) related to accretion (amortization) of the discount (premium) on marketable securities.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the periods indicated (in thousands):

	Year Ended December 31,		
	2022	2021	$ Change
Operating expenses:			
Research and development	$ 62,713	$ 27,996	$ 34,717
General and administrative	20,921	13,671	7,250
Total operating expenses	83,634	41,667	41,967
Loss from operations	(83,634)	(41,667)	(41,967)
Interest and other income, net	1,806	100	1,706
Net loss	$ (81,828)	$ (41,567)	$ (40,261)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the periods indicated (in thousands):

	Year Ended December 31,		
	2022	2021	$ Change
External costs	$ 37,846	$ 17,028	$ 20,818
Internal costs:			
Personnel-related expenses (including stock-based compensation)	19,361	7,853	11,508
Facilities and other allocated expenses	5,506	3,115	2,391
Total research and development expenses	$ 62,713	$ 27,996	$ 34,717

Research and development expenses increased by $34.7 million during the year ended December 31, 2022 compared to the year ended December 31, 2021. The increase of $20.8 million in external costs was primarily driven by an increase of $13.0 million related to clinical and preclinical activities and $7.2 million related to manufacturing activities. Personnel-related expenses, including stock-based compensation, increased by $11.5 million due to an increase in headcount. Facilities and other allocated expenses increased by $2.4 million primarily due to new lease agreements for additional office and laboratory space in Redwood City and San Carlos which commenced in 2021.

General and Administrative Expenses

General and administrative expenses increased by $7.3 million during the year ended December 31, 2022 compared to the year ended December 31, 2021. The increase was primarily due to increased personnel-related expenses, including stock-based compensation, of $4.2 million due to an increase in headcount. Professional services and administrative expenses increased by $2.3 million due to legal, accounting, consulting and other services incurred as a public company.

Interest and Other Income, Net

Interest and other income, net was $1.8 million for the year ended December 31, 2022 compared to $0.1 million for the year ended December 31, 2021. The increase of $1.7 million was primarily due to interest earned from cash and investment balances.

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the periods indicated (in thousands):

	Year Ended December 31,		
	2021	2020	$ Change
Operating expenses:			
Research and development	$ 27,996	$ 3,671	$ 24,325
General and administrative	13,671	1,656	12,015
Total operating expenses	41,667	5,327	36,340
Loss from operations	(41,667)	(5,327)	(36,340)
Interest and other income, net	100	3	97
Net loss	$ (41,567)	$ (5,324)	$ (36,243)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the periods indicated (in thousands):

	Year Ended December 31,		
	2021	2020	$ Change
External costs	$ 17,028	$ 2,748	$ 14,280
Internal costs:			
Personnel-related expenses (including stock-based compensation)	7,853	636	7,217
Facilities and other allocated expenses	3,115	287	2,828
Total research and development expenses	$ 27,996	$ 3,671	$ 24,325

Research and development expenses were $28.0 million for the year ended December 31, 2021, compared to $3.7 million for the year ended December 31, 2020. The increase of $24.3 million was primarily due to an increase in personnel-related expenses, as well as an increase in preclinical and clinical development costs, including manufacturing and external consulting, related to our lead product candidate, BMF-219.

General and Administrative Expenses

General and administrative expenses were $13.7 million for the year ended December 31, 2021, compared to $1.7 million for the year ended December 31, 2020. The increase of $12.0 million was primarily due to increased personnel-related expenses and other corporate costs to support our expanding operations, including legal and accounting, as well as additional costs we have incurred as a public company.

Interest and Other Income, Net

Interest and other income, net was $0.1 million for the year ended December 31, 2021 compared to $3,000 for the year ended December 31, 2020. The increase of $0.1 million was primarily due to interest earned from higher cash and investment balances.

Liquidity and Capital Resources

Liquidity

We have funded our operations primarily through the sale and issuance of shares of our common and convertible preferred stock and the issuance of unsecured promissory notes from inception through December 2020. In April 2021, we completed our IPO and issued an aggregate of 9,000,000 shares of our common stock at a price of $17.00 per share. Following the close of the IPO, an additional 823,532 shares were issued in connection with the partial exercise by the underwriters of their

option to purchase additional shares of common stock. Proceeds from the IPO, net of underwriting discounts and commissions and offering costs, were $152.8 million.

As of December 31, 2022, we had cash, cash equivalents, restricted cash, and investments of $113.4 million. As of December 31, 2022, we had an accumulated deficit of $131.6 million. We have incurred substantial operating losses and have used cash in our operating activities since inception. Without any future financing, the current operating plan under the existing cash and cash equivalents, restricted cash, and investments as of December 31, 2022, will not be sufficient for us to fund our operating expenses and capital expenditure requirements for at least twelve months following the issuance date of the financial statements. Our ability to continue as a going concern will require us to obtain additional financing to fund our operations and there can be no assurance that additional financing will be available to us or that such financing, if available, will be available on terms acceptable to us. Accordingly, there is substantial doubt about our ability to continue as a going concern.

On October 14, 2022, we filed a shelf registration statement on Form S-3 (the Shelf Registration Statement) with the SEC relating to the registration of up to an aggregate of $350.0 million in shares of our common stock, preferred stock, debt securities, warrants and units or any combination thereof. The Shelf Registration Statement was declared effective by the SEC on October 24, 2022. To date, we have not issued any securities or received any proceeds from the sale of any securities registered pursuant to the Shelf Registration Statement.

Future Funding Requirements

We will continue to require additional capital to develop our product candidates and fund operations for the foreseeable future. We may seek to raise capital through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the scope, timing, progress, duration, costs and results of our drug discovery, preclinical development activities, laboratory testing and clinical trials for our product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the extent to which we discover and develop additional product candidates;
- the cost, timing and outcome of regulatory review of our product candidates;
- the cost and timing of establishing sales and marketing capabilities, if any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- licensing, or other arrangements into which we may enter in the future, including the timing of receipt of any milestone or royalty payments under these agreements;
- the timing, receipt and amount of sales from our potential products;
- our need and ability to hire additional management, scientific and medical personnel;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company;
- the cost associated with commercializing our product candidates, if they receive regulatory approval;
- our ability to establish and maintain strategic collaborations and other similar partnerships for the development and commercialization of our product candidates; and

- the impact of the ongoing COVID-19 pandemic and adverse global economic conditions on our business, which may exacerbate the magnitude of the factors discussed above.

If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license to others rights to our product candidates in certain territories or indications that we would prefer to develop and commercialize ourselves.

See the section of this Annual Report on Form 10-K titled "Risk Factors" for additional risks associated with our substantial capital requirements.

Summary Statement of Cash Flows

The following table sets forth the primary sources and uses of cash, cash equivalents and restricted cash for each of the periods presented below (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Net cash (used in) provided by:			
Operating activities	$ (62,417)	$ (35,438)	$ (4,459)
Investing activities	27,341	(33,355)	(51)
Financing activities	1,239	153,185	65,966
Net increase in cash, cash equivalents, and restricted cash	$ (33,837)	$ 84,392	$ 61,456

Net Cash Used in Operating Activities

Net cash used in operating activities was $62.4 million for the year ended December 31, 2022. Cash used in operating activities in 2022 was mainly the result of the net loss of $81.8 million and increase in prepaid expenses and other assets of $3.6 million. This was offset by an increase in accounts payable and accrued liabilities of $11.9 million and stock-based compensation expense of $10.3 million.

Net cash used in operating activities was $35.4 million for the year ended December 31, 2021. Cash used in operating activities in 2021 was mainly the result of the net loss of $41.6 million and increase in prepaid expenses and other assets of $3.7 million. This was offset by an increase in accounts payable and accrued liabilities of $2.8 million and stock-based compensation expense of $6.2 million.

Net cash used in operating activities was $4.5 million for the year ended December 31, 2020. Cash used in operating activities in 2020 was primarily due to the use of funds in our operations and the resulting net loss of $5.3 million, offset by an aggregate increase in our accounts payable and accrued liabilities balance of $1.0 million.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $27.3 million for the year ended December 31, 2022. Cash provided by investing activities was mainly related to maturities of investments offset by purchases of property and equipment.

Net cash used in investing activities was $33.4 million for the year ended December 31, 2021. Cash used in investing activities in 2021 was mainly related to cash investments in securities and purchases of property and equipment.

Net cash used in investing activities was $51,000 for the year ended December 31, 2020. Cash used in investing activities in 2020 was mainly related to purchases of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $1.2 million for the year end December 31, 2022. Cash provided by financing activities was mainly related to proceeds received from stock option exercises and purchases under the employee stock purchase plan.

Net cash provided by financing activities was $153.2 million for the year ended December 31, 2021. This was primarily related to $152.8 million of net proceeds received from the issuance of common stock from our initial public offering.

Net cash provided by financing activities was $66.0 million for the year ended December 31, 2020, which consisted of $10.2 million of net proceeds from the issuance and sale of shares of our common stock, and $55.7 million of net proceeds from the issuance and sale of shares of our convertible preferred stock.

Critical Accounting Estimates

Our financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist primarily of personnel costs for our research and product development employees. Also included are non-personnel costs such as fees payable to third parties for clinical and preclinical studies and research services, laboratory supplies, equipment maintenance, and other consulting costs.

We record accruals for estimated costs of research, preclinical studies, clinical trials, and manufacturing, which are significant components of research and development expenses. A substantial portion of our ongoing research and development activities is conducted by third-party service providers, CROs and CMOs. Our contracts with the CMOs generally include fees such as initiation fees, reservation fees, costs related to animal studies and safety tests, verification run costs, materials and reagents expenses, taxes, etc. Our contracts with CROs generally include pass-through fees such as regulatory expenses, investigator fees, travel costs and other miscellaneous costs, including shipping and printing fees. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts. We accrue the costs incurred under agreements with these third parties based on estimates of actual work completed in accordance with the respective agreements. We determine the estimated costs through discussions with internal personnel and external service providers as to the progress, or stage of completion or actual timeline (start-date and end-date) of the services and the agreed-upon fees to be paid for such services. In the event we make advance payments, the payments are recorded as a prepaid expense and recognized as the services are performed.

Stock-Based Compensation

We measure stock options and other stock-based awards granted to directors, employees and non-employees based on their fair value on the date of the grant and recognize the corresponding compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We have only issued stock options and restricted share awards with service-based vesting conditions and record the expense for these awards using the straight-line method. We determine the fair value of restricted stock awards granted based on the fair value of our common stock. Forfeitures are accounted for as they occur.

We estimate the fair value of each stock option grant using the Black-Scholes option pricing model, which uses as inputs the following assumptions:

- *Fair value of common stock* - See the subsection titled "Fair Value of Common Stock" below.
- *Expected term* - The expected term represents the period that the stock-based awards are expected to be outstanding. We use the simplified method to determine the expected term, which is based on the average of the time-to-vesting and the contractual life of the options.
- *Expected volatility* - Because we have been privately held and do not have any trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on the similar size, stage in life cycle or area of specialty. We will continue to take this approach until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- *Risk-free interest rate* - The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the awards.

- *Dividend yield* - We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

Assumptions we used in applying the Black-Scholes option-pricing model to determine the estimated fair value of our stock options granted involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation could be materially different.

Fair Value of Common Stock

Historically, for all periods prior to our IPO, the fair value of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, timely valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provide by the American Institute of Certified Public Accountants Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Given the absence of a public trading market for our common stock prior to our IPO, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

Since the completion of our IPO, the fair value of each share of common stock underlying stock option grants is based on the closing price of our common stock on the Nasdaq Global Select Market as reported on the date of grant.

Leases

We determine if an arrangement is a lease at inception. In addition, we determine whether leases meet the classification criteria of a finance or operating lease at the lease commencement date considering: (1) whether the lease transfers ownership of the underlying asset to the lessee at the end of the lease term, (2) whether the lease grants the lessee an option to purchase the underlying asset that the lessee is reasonably certain to exercise, (3) whether the lease term is for a major part of the remaining economic life of the underlying asset, (4) whether the present value of the sum of the lease payments and residual value guaranteed by the lessee equals or exceeds substantially all of the fair value of the underlying asset, and (5) whether the underlying asset is of such a specialized nature that it is expected to have no alternative use to the lessor at the end of the lease term. As of December 31, 2022, our lease population consisted of real estate operating leases.

Operating leases are included in operating lease right-of-use (ROU) assets, lease liabilities, current, and lease liabilities, non-current in our balance sheet. ROU assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. In determining the present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date if the rate implicit in the lease is not readily determinable. We determine the incremental borrowing rate base on an analysis of corporate bond yields with a credit rating similar ours. The determination of our incremental borrowing rate requires management judgment including the development of a synthetic credit rating and cost of debt as we currently do not carry any debt. We believe that the estimates used in determining the incremental borrowing rate are reasonable based upon current facts and circumstances. Applying different judgments to the same facts and circumstances could result in the estimated amounts to vary. The operating lease ROU assets also include adjustments for prepayments and accrued lease payments and exclude lease incentives. Our lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise such options. Operating lease cost is recognized on a straight-line basis over the expected lease term. Lease agreements entered into after the adoption of ASC 842 that include lease and non-lease components are accounted for as a single lease component. Lease agreements with a noncancelable term of less than 12 months are not recorded on our balance sheet.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

The primary objectives of our investment activities are to ensure liquidity and to preserve capital. We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. There was no material foreign currency risk for the year ended December 31, 2022. We held $113.4 million in cash, cash equivalents, restricted cash, and investments as of December 31, 2022. Cash equivalents and investments consisted of money market funds, commercial paper, and corporate debt. Restricted cash consisted of a stand-by letter of credit issued to our landlord in connection with the lab lease. We held no interest-bearing liabilities as of December 31, 2022. Historical fluctuations in interest rates have not been significant for us. Due to the short-term maturities of our cash equivalents, an immediate 10% relative change in interest rates would not have a material effect on the fair market value of our cash equivalents.

Item 8. Financial Statements and Supplementary Data

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Biomea Fusion, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Biomea Fusion, Inc. (the "Company") as of December 31, 2022 and 2021, the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has incurred net operating losses and negative cash flows from operations that raise substantial doubt about its ability to continue as a going concern. Management's evaluation of the events and conditions and their plan regarding these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ *DELOITTE & TOUCHE LLP*

San Francisco, California

March 28, 2023

We have served as the Company's auditor since 2020.

Biomea Fusion, Inc.
Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2022	**2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 111,899	$ 145,736
Short-term investments	1,150	27,780
Prepaid expenses and other current assets	4,770	3,045
Total current assets	117,819	176,561
Property and equipment, net	5,841	2,965
Restricted cash	351	351
Other assets	3,145	1,230
Long-term investments	—	1,876
Operating lease right-of-use assets	2,151	2,722
Total assets	$ 129,307	$ 185,705
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 6,826	$ 1,329
Accrued expenses and other current liabilities	11,657	2,743
Operating lease liabilities, current	618	565
Total current liabilities	19,101	4,637
Operating lease liabilities, non-current	1,667	2,285
Total liabilities	20,768	6,922
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 authorized as of December 31, 2022 and December 31, 2021; 0 shares issued and outstanding as of December 31, 2022 and December 31, 2021	—	—
Common stock, $0.0001 par value; 300,000,000 authorized as of December 31, 2022 and December 31, 2021; 29,561,554 and 29,115,421 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	3	3
Additional paid-in capital	240,107	228,532
Accumulated other comprehensive loss	(1)	(10)
Accumulated deficit	(131,570)	(49,742)
Total stockholders' equity	108,539	178,783
Total liabilities and stockholders' equity	$ 129,307	$ 185,705

The accompanying notes are an integral part of these financial statements.

Biomea Fusion, Inc.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,		
	2022	**2021**	**2020**
Operating expenses:			
Research and development	$ 62,713	$ 27,996	$ 3,671
General and administrative	20,921	13,671	1,656
Total operating expenses	83,634	41,667	5,327
Loss from operations	(83,634)	(41,667)	(5,327)
Interest and other income, net	1,806	100	3
Net loss	$ (81,828)	$ (41,567)	$ (5,324)
Other comprehensive loss:			
Unrealized gain (loss) on investments, net	9	(10)	—
Comprehensive loss	$ (81,819)	$ (41,577)	$ (5,324)
Net loss per share, basic and diluted	$ (2.80)	$ (1.74)	$ (0.51)
Weighted-average number of common shares used to compute basic and diluted net loss per common share	29,271,777	23,858,552	10,532,942

The accompanying notes are an integral part of these financial statements.

Biomea Fusion, Inc.
Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Series A Convertible Preferred Stock		Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Gain (Loss)	Deficit	Equity (Deficit)
Balance at December 31, 2019	**—**	**—**	**8,703,234**	**1**	**2,829**	**—**	**(2,851)**	**(21)**
Issuance of Series A convertible preferred stock, net of issuance costs of $261	7,064,925	55,738	—	—	—	—	—	—
Issuance of common stock, net of issuance costs of $68	—	—	3,175,279	—	10,192	—	—	10,192
Issuance of restricted stock	—	—	74,594	—	—	—	—	—
Stock-based compensation	—	—	—	—	322	—	—	322
Net loss	—	—	—	—	—	—	(5,324)	(5,324)
Balance at December 31, 2020	**7,064,925**	**55,738**	**11,953,107**	**1**	**13,343**	**—**	**(8,175)**	**5,169**
Series A convertible preferred stock issuance costs	—	(3)	—	—	—	—	—	—
Issuance of common stock from initial public offering, net of issuance costs of $2,557	—	—	9,823,532	1	152,753	—	—	152,754
Conversion of Series A convertible preferred stock into common stock	(7,064,925)	(55,735)	7,064,925	1	55,734	—	—	55,735
Issuance of restricted stock	—	—	204,187	—	—	—	—	—
Exercise of stock options	—	—	48,663	—	254	—	—	254
Purchases under employee stock purchase plan	—	—	21,007	—	214	—	—	214
Stock-based compensation	—	—	—	—	6,234	—	—	6,234
Unrealized gain (loss) on investments, net	—	—	—	—	—	(10)	—	(10)
Net loss	—	—	—	—	—	—	(41,567)	(41,567)
Balance at December 31, 2021	**—**	**—**	**29,115,421**	**3**	**228,532**	**(10)**	**(49,742)**	**178,783**
Issuance of restricted stock	—	—	186,727	—	—	—	—	—
Exercise of stock options	—	—	81,067	—	516	—	—	516
Purchases under employee stock purchase plan	—	—	178,339	—	723	—	—	723
Stock-based compensation	—	—	—	—	10,336	—	—	10,336
Unrealized gain (loss) on investments, net	—	—	—	—	—	9	—	9
Net loss	—	—	—	—	—	—	(81,828)	(81,828)
Balance at December 31, 2022	**—**	**$ —**	**29,561,554**	**$ 3**	**$ 240,107**	**$ (1)**	**$ (131,570)**	**$ 108,539**

The accompanying notes are an integral part of these financial statements.

Biomea Fusion, Inc.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Cash flows from operating activities			
Net loss	$ (81,828)	$ (41,567)	$ (5,324)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation expense	691	249	8
Non-cash operating lease expense	571	704	124
Stock-based compensation expense	10,336	6,234	322
Net amortization of premiums and accretion of discounts on investments	144	516	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(1,725)	(2,517)	(472)
Other assets	(1,915)	(1,218)	(12)
Accounts payable	2,960	640	418
Accrued expenses and other current liabilities	8,914	2,110	588
Operating lease liabilities	(565)	(589)	(111)
Net cash used in operating activities	(62,417)	(35,438)	(4,459)
Cash flows from investing activities			
Purchase of property and equipment	(1,030)	(3,171)	(51)
Purchase of investments	—	(38,492)	—
Maturities of investments	28,371	8,308	—
Net cash provided by (used in) investing activities	27,341	(33,355)	(51)
Cash flows from financing activities			
Proceeds from issuance of common stock, net of issuance costs	—	—	10,192
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs	—	—	55,738
Proceeds from issuance of common stock from initial public offering, net of issuance costs	—	152,753	—
Proceeds from exercise of stock options and purchases under the employee stock purchase plan	1,239	468	—
Proceeds (payment) from Paycheck Protection Program loan	—	(36)	36
Net cash provided by financing activities	1,239	153,185	65,966
Net increase in cash, cash equivalents, and restricted cash	(33,837)	84,392	61,456
Cash, cash equivalents, and restricted cash at the beginning of the period	146,087	61,695	239
Cash, cash equivalents, and restricted cash at the end of the period	$ 112,250	$ 146,087	$ 61,695
Non-cash financing and investing activities:			
Acquisition of operating lease right-of-use assets	$ —	$ 3,216	$ 334
Acquisition of property and equipment included in accounts payable and accrued expenses and other current liabilities	$ 2,537	$ —	$ 38
Unpaid deferred offering costs	$ —	$ —	$ 29
Reconciliation of cash, cash equivalents, and restricted cash:			
Cash and cash equivalents	111,899	145,736	61,695
Restricted cash	351	351	—
Total cash, cash equivalents, and restricted cash	$ 112,250	$ 146,087	$ 61,695

The accompanying notes are an integral part of these financial statements.

Biomea Fusion, Inc.
Notes to Financial Statements

Note 1. Organization

Organization

Biomea Fusion, Inc., (the Company), was established in the state of Delaware in August 2017 as Biomea Fusion, LLC. In December 2020, all outstanding membership interests in Biomea Fusion, LLC were converted into equity interests in the Company. The capitalization information included in these financial statements is consistently presented as if it is that of Biomea Fusion, Inc., even during the prior period when investors held their equity interests in Biomea Fusion, LLC.

The Company is a clinical-stage biopharmaceutical company dedicated to discovering and developing novel covalent small molecules to treat and improve the lives of patients with genetically defined cancers and metabolic diseases. Since its inception in 2017, the Company has built its proprietary FUSION™ System platform to design and develop a pipeline of novel covalent product candidates.

Forward Stock Split

In April 2021, the Company's board of directors approved an amended and restated certificate of incorporation to effect a split of shares of the Company's outstanding capital at a ratio of 8.84-for-1 (the Forward Stock Split) effective as of April 12, 2021. The number of authorized shares and the par values of the common stock and convertible preferred stock were not adjusted as a result of the Forward Stock Split. All references to common stock, options to purchase common stock, convertible preferred stock, share data, per share data and related information contained in the financial statements have been retrospectively adjusted to reflect the effect of the Forward Stock Split for all periods presented.

Initial Public Offering

On April 16, 2021, the Company's registration statement on Form S-1 (File No. 333-254793) relating to its initial public offering (IPO) of common stock became effective. The IPO closed on April 20, 2021 at which time the Company issued an aggregate of 9,000,000 shares of its common stock at a price of $17.00 per share. Subsequent to the close, an additional 823,532 shares were issued in connection with the partial exercise by the underwriters of their option to purchase additional shares of common stock. In addition, immediately prior to the closing of the IPO, all outstanding shares of the Company's convertible preferred stock automatically converted into 7,064,925 shares of common stock. In connection with the completion of its IPO, on April 20, 2021, the Company's certificate of incorporation was amended and restated to provide for 300,000,000 authorized shares of common stock with a par value of $0.0001 per share and 10,000,000 authorized shares of preferred stock with a par value of $0.0001 per share. Proceeds from the IPO, net of underwriting discounts and commissions and offering costs, were $152.8 million.

Liquidity and Capital Resources

The accompanying financial statements have been prepared assuming the Company will continue as a going concern, which assumes the realization of assets and satisfaction of liabilities and commitments in the normal course of business. The Company believes that based on its current operating plan, its cash and cash equivalents, restricted cash, and investments will not enable it to fund its operating expenses and capital expenditure requirements for at least twelve months following the issuance date of the financial statements. The Company's ability to continue as a going concern will require the Company to raise additional capital to fund the Company's operations through public or private equity offering, debt financings, collaborations and licensing arrangements or other sources. There can be no assurance that additional financing will be available to the Company or that such financing, if available, will be available on terms acceptable to the Company. Accordingly, there is substantial doubt about the Company's ability to continue as a going concern. The Company has incurred net operating losses and negative cash flows from operations since its inception and had an accumulated deficit of $131.6 million at December 31, 2022. As of December 31, 2022, the Company had cash, cash equivalents, restricted cash, and investments of $113.4 million.

The Company has historically financed its operations primarily through the sale of convertible preferred stock and common stock and the issuance of unsecured promissory notes. To date, none of the Company's product candidates have been approved for sale, and the Company has not generated any revenue since inception. Management expects operating losses to continue and increase for the foreseeable future, as the Company progresses into clinical development activities for its lead product candidate and advances the preclinical and clinical development of other product candidates. The Company's prospects are subject to risks, expenses and uncertainties frequently encountered by companies in the biotechnology industry.

Failure to generate sufficient cash flows from operations or raise additional capital would have a material adverse effect on the Company's ability to achieve its intended business objectives.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation

These financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (U.S. GAAP).

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company evaluates its estimates, including, but not limited to, those related to clinical and preclinical accruals, manufacturing accruals, fair value of common stock, stock-based compensation, operating lease right-of-use (ROU) assets and liabilities and income taxes. The Company bases its estimates on its historical experience and also on assumptions that it believes are reasonable; however, actual results could significantly differ from those estimates.

Segments

The Company operates and manages its business as one reportable and operating segment, which is the business of developing covalent small molecule drugs to treat patients with genetically defined cancers and metabolic diseases. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for allocating resources and evaluating financial performance. All long-lived assets are maintained in, and all losses are attributable to, the United States of America.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk, consist primarily of cash, cash equivalents and investments. The Company maintains bank deposits in federally insured financial institutions and these deposits may exceed federally insured limits. The Company invests in money market funds, U.S. Treasury securities, U.S. government agency securities, corporate notes, commercial paper, and asset backed securities. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents and issuers of investments to the extent recorded in the balance sheet. The Company's investment policy limits investments to money market funds, certain types of debt securities issued by the U.S. Government and its agencies, corporate notes and commercial paper, and places restrictions on the credit ratings, maturities and concentration by type and issuer. The Company has not experienced any losses on its deposits of cash, cash equivalents and investments.

Other Risks and Uncertainties

The Company's future results of operations involve a number of other risks and uncertainties. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations include, but are not limited to, uncertainty of results of preclinical studies, clinical trials and achievement of milestones, uncertainty of regulatory approval of the Company's potential product candidates, uncertainty of market acceptance of the Company's product candidates, competition from substitute products and larger companies, securing and protecting proprietary technology, strategic relationships and dependence on key individuals or sole source suppliers and changes in the Company's operating expenses as a result of these uncertainties and other factors, such as inflation. The Company's product candidates require approvals from the U.S. Food and Drug Administration and comparable foreign regulatory agencies prior to commercial sales in their respective jurisdictions. There can be no assurance that any product candidates will receive the necessary approvals. If the Company is denied approval, approval is delayed or the Company is unable to maintain approval for any product candidate, it could have a materially adverse impact on the Company.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments with original maturities of three months or less from the date of purchase to be cash and cash equivalents. Cash equivalents consist of amounts invested in money market accounts and are stated at fair value. Restricted cash consists of two stand-by letters of credit issued to the Company's landlord in connection with two of the Company's leases.

Investments

The Company's investments have been classified and accounted for as available-for-sale securities. Fixed income securities consist of U.S. Treasury securities, U.S. government agency securities, corporate debt securities, commercial paper and asset backed securities. The specific identification method is used to determine the cost basis of fixed income securities sold. These securities are recorded on the balance sheets at fair value. Unrealized gains and losses on these securities are included as a separate component of accumulated other comprehensive loss. The cost of investment securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in other income (expense), net. Realized gains and losses and declines in fair value judged to be other-than-temporary, if any, are also included in other income (expense), net. The Company evaluates securities for other-than-temporary impairment at the balance sheet date. Declines in fair value determined to be other-than-temporary are also included in other income (expense), net. The Company classifies its investments with the remaining effective maturities of twelve months or less from the balance sheet date are classified as short-term; otherwise, they are classified as long-term on the balance sheet.

Property and Equipment, Net

Property and equipment are recorded at cost net of accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets. The useful lives of property and equipment are as follows:

Computer equipment	3 years
Furniture and fixtures	5 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

Upon retirement or sale of the assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is recorded to the statements of operations. Repairs and maintenance are expensed as incurred.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future net cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset. There was no impairment of long-lived assets during the years ended December 31, 2022, 2021 and 2020.

Research and Development Expenses

The Company expenses research and development costs as they are incurred. Research and development expenses consist primarily of: (i) personnel-related expenses, including salaries, benefits and stock-based compensation expense, for personnel in the Company's research and development functions; (ii) fees paid to third parties such as contractors, consultants and contract research organizations (CROs), for animal studies and other costs related to preclinical and clinical testing; (iii) costs related to acquiring and manufacturing research and clinical trial materials, including under agreements with third parties such as contract manufacturing organizations (CMOs), and other vendors; (iv) costs related to the preparation of regulatory submissions; (v) expenses related to laboratory supplies and services; and (vi) depreciation of equipment and facilities expenses.

Accrued Research and Development Expenses

The Company records accruals for estimated costs of research, preclinical studies, clinical trials, and manufacturing development, which are significant components of research and development expenses. A substantial portion of the Company's ongoing research and development activities is conducted by third-party service providers, CROs and CMOs. The Company's contracts with the CROs and CMOs generally include fees such as initiation fees, reservation fees, costs related to animal studies and safety tests, verification run costs, materials and reagents expenses, investigator fees, taxes, etc. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts. The Company accrues the costs incurred under agreements with these third parties based on estimates of actual work completed in accordance with the respective agreements. The Company determines the estimated costs through discussions with internal personnel and external service providers as to the progress, or stage of completion and actual timeline (start-date and end-date) of the services and the agreed-upon fees to be paid for such services. Through December

31, 2022, there have been no material differences from the Company's estimated accrued research and development expenses to actual expenses.

Stock-Based Compensation

The Company accounts for stock-based compensation by measuring and recognizing compensation expense for all share-based awards made to employees, non-employees and directors based on estimated grant-date fair values. The Company uses the straight-line method to allocate compensation cost to reporting periods over the requisite service period, which is generally the vesting period, and estimates the fair value of share-based awards to employees, non-employees and directors using the Black-Scholes option-pricing model. The Company accounts for forfeitures as they occur. The fair value of restricted stock awards is based on grant-date fair value. The fair value of each purchase under the employee stock purchase plan (ESPP) is estimated at the beginning of the offering period using the Black-Scholes option pricing model and recorded as expense over the service period using the straight-line method.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

Leases

The Company determines if an arrangement is a lease at inception in accordance with Accounting Standard Codification 842, "Leases" (ASC 842). As of December 31, 2022, the Company's lease population consisted of real estate leases and the Company did not have finance leases.

Operating leases are included in operating lease right-of-use (ROU) assets, current operating lease liabilities and non-current operating lease liabilities on the Company's balance sheet. ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. As most of the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of those lease payments. The Company determines the incremental borrowing rate based on an analysis of corporate bond yields with a credit rating similar to the Company. The determination of the Company's incremental borrowing rate requires management judgment including the development of a synthetic credit rating and cost of debt as the Company currently does not carry any debt. The Company believes that the estimates used in determining the incremental borrowing rate are reasonable based upon current facts and circumstances. Applying different judgments to the same facts and circumstances could result in the estimated amounts to vary. The operating lease ROU assets also include adjustments for prepayments and accrued lease payments and exclude lease incentives. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise such options. Operating lease cost is recognized on a straight-line basis over the expected lease term. Variable lease costs represent payments that are dependent on usage, a rate or index. Variable lease cost primarily relates to common area maintenance charges. Lease agreements that include lease and non-lease components are accounted for as a single lease component. The Company has elected to apply the short-term lease exception for all lease agreements with a noncancelable term of less than 12 months.

Income Taxes

The Company began providing for income taxes under the asset and liability method in December 2020 upon conversion from a limited liability company into a corporation. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax basis of assets and liabilities and net operating loss and credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all the tax benefits will not be realized.

The Company accounts for uncertain tax positions in accordance with ASC No. 740 *Income Taxes*. The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be

reassessed, and the Company will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

The Company includes any penalties and interest expense related to income taxes as a component of income tax expense, as necessary.

Recent Accounting Pronouncements - Adopted

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740)—Simplifying the Accounting for Income Taxes* (ASU 2019-12), which is intended to simplify accounting for income taxes. It removes certain exceptions to the general principles in Topic 740 and amends existing guidance to improve consistent application. The Company adopted ASU 2019-12 as of January 1, 2022 on a prospective basis and there was no impact on the Company's financial statements and disclosures as a result of this adoption.

Recent Accounting Pronouncements - Not Yet Adopted

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which requires that financial assets measured at amortized cost be presented at the net amount expected to be collected. The measurement of expected credit losses is based on historical experience, current conditions, and reasonable and supportable forecasts that affect collectability. This ASU also eliminates the concept of "other-than-temporary" impairment when evaluating available-for-sale debt securities and instead focuses on determining whether any impairment is a result of a credit loss or other factors. An entity will recognize an allowance for credit losses on available-for-sale debt securities rather than an other-than-temporary impairment that reduces the cost basis of the investment. This ASU is effective for fiscal years beginning after December 15, 2022 and interim periods within those fiscal years. The Company plans to adopt this ASU on January 1, 2023. The Company does not expect the adoption of this standard to have a material impact on its financial statements and related disclosures.

Note 3. Fair Value Measurement

The Company applies fair value accounting for all financial assets and liabilities. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

Level 1—Observable inputs, such as quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs which reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

In determining fair value, the Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

The carrying amount of cash and cash equivalents, prepaid expenses, accounts payable and accrued expenses are generally considered to be representative of their respective fair values because of the short-term nature of these instruments.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company classifies money market funds as Level 1 within the fair value hierarchy as the fair value is based on quoted price in active markets. The Company classifies its investments in corporate debt securities, commercial paper and asset backed securities as Level 2 within the fair value hierarchy as the fair value is based on other observable inputs, including broker or dealer quotations or alternative pricing sources. When quoted prices in active markets

for identical assets or liabilities are not available, the Company relies on non-binding quotes from its investment managers, which are based on proprietary valuation models of independent pricing services. These models generally use inputs such as observable market data, quoted market prices for similar instruments, or historical pricing trends of a security relative to its peers. To validate the fair value determination provided by its investment managers, the Company reviews the pricing movement in the context of overall market trends and trading information from its investment managers. In addition, the Company assesses the inputs and methods used in determining the fair value in order to determine the classification of securities in the fair value hierarchy. As of December 31, 2022 and 2021, there were no financial instruments classified as Level 3. The Company evaluates transfers between levels at the end of each reporting period and there were no transfers of financial instruments between the fair value measurement levels during the year ended December 31, 2022.

As of December 31, 2022, investments measured and recognized at fair value are as follows (in thousands):

		December 31, 2022			
	Fair Value Hierarchy Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Financial assets included within cash and cash equivalents:					
Money market funds	Level 1	$ 105,684	$ —	$ —	$ 105,684
Financial assets included within short-term investments:					
Corporate notes	Level 2	1,151	—	(1)	1,150
Total		$ 106,835	$ —	$ (1)	$ 106,834

As of December 31, 2022, the weighted average remaining contractual maturity for available-for-sale securities was 0.4 month.

		December 31, 2021			
	Fair Value Hierarchy Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Financial assets included within cash and cash equivalents:					
Money market funds	Level 1	$ 112,193	$ —	$ —	$ 112,193
Financial assets included within short-term investments:					
Corporate notes	Level 2	19,258	1	(6)	19,253
Commercial paper	Level 2	4,499	—	—	4,499
Asset backed securities	Level 2	4,029	—	(1)	4,028
Financial assets included within long-term investments:					
Corporate notes	Level 2	1,185	—	(4)	1,181
Asset backed securities	Level 2	695	—	—	695
Total		$ 141,859	$ 1	$ (11)	$ 141,849

Note 4. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net consists of the following (in thousands):

	December 31,	
	2022	2021
Laboratory equipment	$ 2,331	$ 1,874
Computer equipment	130	124
Furniture and fixtures	325	315
Leasehold improvements	801	828
Construction in progress	3,170	81
Total property and equipment, gross	6,757	3,222
Less: accumulated depreciation	(916)	(257)
Total property and equipment, net	$ 5,841	$ 2,965

Depreciation expense was approximately $0.7 million, $0.2 million and $8,000 for the years ended December 31, 2022, 2021 and 2020, respectively.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2022	2021
Accrued research and development materials and services	$ 6,039	$ 1,674
Accrued professional services	208	170
Accrued personnel expenses	4,774	419
Other	636	480
Total accrued expenses and other current liabilities	$ 11,657	$ 2,743

Note 5. Capital Structure

Common Stock

In December 2020, all of the outstanding membership interests in Biomea Fusion LLC were exchanged for equity interests in Biomea Fusion, Inc. in a statutory conversion under Delaware law. All of the share information referenced throughout the financial statements and notes to the financial statements have been retroactively adjusted to reflect the change in capital structure.

In connection with the completion of its IPO, on April 20, 2021, the Company's certificate of incorporation was amended and restated to authorize 300,000,000 shares of common stock with a par value of $0.0001 per share and 10,000,000 shares of preferred stock with a par value of $0.0001 per share.

Common stockholders are entitled to dividends when and if declared by the Company's Board of Directors and after any preferred share dividends are fully paid. The holder of each share of common stock is entitled to one vote. As of December 31, 2022 and 2021, no dividends have been declared.

The Company had reserved common stock, on an as-converted basis, for future issuance as follows:

	December 31,	
	2022	2021
Stock options, issued and outstanding	5,341,975	4,254,504
Stock options, authorized for future issuance	1,446,872	1,134,944
Employee stock purchase plan, available for future issuance	402,747	284,993
Restricted stock, issued and outstanding	292,236	493,914
Total	7,483,830	6,168,355

Note 6. Stock-Based Compensation

2020 Equity Incentive Plan

The Company adopted the 2020 Equity Incentive Plan (the "2020 Plan") on December 18, 2020. The 2020 Plan reserved 4,327,799 shares of common stock to grant stock-based compensation awards, including stock options and restricted stock awards, to employees and non-employees. As of April 9, 2021, the Company ceased granting awards under the 2020 Plan. However, 2020 Plan awards will remain subject to the terms of the 2020 Plan.

2021 Equity Incentive Plan

In April 2021, the Company adopted the 2021 Equity Incentive Plan (the "2021 Plan"). Options granted under the 2021 Plan expire no later than 10 years from the date of grant. The exercise price of options granted under the 2021 Plan must at least be equal to the fair market value of the Company's common stock on the date of grant. With respect to any participant who owns more than 10% of the voting power of all classes of the Company's outstanding stock, the term of an incentive stock option granted to such participant must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. Employee stock options generally vest $1/16^{th}$ quarterly over four years subject to continued service to the Company.

Subject to adjustment in the case of certain capitalization events as provided in the 2021 Plan, the Company initially reserved 3,370,000 shares of the Company's common stock for issuance pursuant to awards under the 2021 Plan. The 2021 Plan is administered by the Compensation Committee of the Company's Board of Directors. The number of shares of the Company's common stock available for issuance under the 2021 Plan will also include an annual increase on the first day of each fiscal year beginning in 2022 and ending in 2031, equal to the lesser of (i) 5% of the Company's common stock outstanding at December 31 of the immediately preceding year, or (ii) such number of shares as determined by the Company's Board of Directors. As of December 31, 2022, 1,446,872 shares of common stock remained available for issuance under the 2021 Plan. Effective January 1, 2023, the number of shares of common stock available under the 2021 Plan increased by 1,493,437 shares pursuant to the evergreen provision of the 2021 Plan.

2021 Employee Stock Purchase Plan

The Company adopted a 2021 Employee Stock Purchase Plan (ESPP) in April 2021. The ESPP enables eligible employees of the Company and designated affiliates to purchase shares of common stock at a discount of 15%. Subject to adjustment in the case of certain capitalization events, a total of 306,000 common shares of the Company were available for purchase at adoption of the ESPP. Pursuant to the ESPP, the annual share increase pursuant to the evergreen provision is determined based on the lesser of (i) 1% of the Company's common stock outstanding at December 31 of the immediately preceding year, or (ii) such number of shares as determined by the Company's Board of Directors. As of December 31, 2022, 402,747 shares of common stock remained available for issuance under the ESPP. Effective January 1, 2023, the number of shares of common stock available under the ESPP increased by 298,687 shares pursuant to the evergreen provision of the ESPP.

Stock-Based Compensation Expense

Total stock-based compensation expense related to the 2020 Plan, 2021 Plan, and ESPP was recorded in the statements of operations and allocated as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Research and development	$ 4,678	$ 2,637	$ 89
General and administrative	5,658	3,597	233
Total stock-based compensation expense	$ 10,336	$ 6,234	$ 322

As of December 31, 2022, there was $25.0 million of total unrecognized compensation cost related to stock options, restricted stock awards, and ESPP under the Plans. The unrecognized stock-based compensation cost is expected to be recognized over a weighted-average period of 2.5 years.

Stock Options

The following table summarizes stock option activity:

	Number of Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Balance as of December 31, 2021	4,254,504	$ 9.89	9.4	$ 1,868
Granted	1,602,909	6.86		
Exercised	(81,067)	6.37		
Cancelled	(434,371)	12.83		
Balance as of December 31, 2022	5,341,975	$ 8.79	8.6	$ 6,875
Options exercisable as of December 31, 2022	1,747,167	$ 8.88	8.3	$ 2,368

The fair value of stock options was estimated using the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Expected term in years	6.0	6.0	—
Expected volatility	93.1%	91.0%	—
Risk-free interest rate	3.1%	1.1%	—
Dividend yield	—	—	—
Weighted average fair value of options granted	$ 5.25	$ 7.28	$ —

The aggregate intrinsic value of options exercised for the years ended December 31, 2022, 2021, 2020 was $0.4 million, $0.5 million, and zero, respectively. Intrinsic values are calculated as the difference between the exercise price of the underlying options and the fair value of the common stock on the date of exercise.

Employee Stock Purchase Plan

The fair value of ESPP was estimated using the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Expected term in years	1.3	1.3	—
Expected volatility	95.2%	91.3%	—
Risk-free interest rate	2.5%	0.3%	—
Dividend yield	—	—	—

Restricted Stock

The Company granted 824,429 restricted stock awards to employees and non-employees during the fourth quarter of 2020 that vest quarterly over four years. Restricted stock awards are share awards that entitle the holder to receive freely tradeable shares of the Company's common stock. The underlying shares are outstanding as of the issuance date. Any unvested shares are subject to forfeiture in the case that the grantee's service terminates prior to vesting of the restricted stock.

The following table summarizes the restricted stock activity:

	Number of Restricted Stock Awards	Weighted-Average Grant Date Fair Value
Balance, December 31, 2021	493,914	$ 4.02
Granted	—	—
Released	(186,727)	4.02
Forfeited	(14,951)	3.96
Balance, December 31, 2022	292,236	$ 4.04

Note 7. Taxes

Biomea Fusion is subject to U.S. federal and state income taxes as a corporation. Prior to the tax-free reorganization in December 2020, Biomea Fusion, LLC was treated as a pass-through entity for U.S. federal income tax purposes, and as such, was generally not subject to U.S. federal income tax at the entity level. Rather, the tax liability with respect to its taxable income, was passed through to its unitholders.

There was zero income tax expense for the years ended December 31, 2022, 2021 and 2020. The following is a reconciliation of the statutory federal income tax rate to the Company's effective tax rate:

	Year Ended December 31,		
	2022	2021	2020
Federal statutory income tax rate	21.0%	21.0%	21.0%
State income tax rate	0.5%	0.5%	1.1%
Tax credits	1.1%	0.2%	—
Stock-based compensation	(1.1)%	(1.5)%	—
Amortization	—	2.6%	—
LLC loss prior to C-Corp conversion	—	—	(17.7)%
Change in valuation allowance	(21.5)%	(22.7)%	(4.3)%
Other	—	(0.1)%	(0.1)%
Effective income tax rate	0.0%	0.0%	0.0%

Deferred tax assets and liabilities consist of the following (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 12,100	$ 7,689
Capitalized research and development	10,326	—
Accrued liabilities and reserves	411	65
Stock-based compensation	1,887	675
Intangible assets	1,129	1,044
Operating lease liabilities	480	599
Research and development credits	1,633	278
Property and equipment	—	—
Gross deferred tax assets	27,966	10,350
Valuation allowance	(27,432)	(9,730)
Total deferred tax assets	534	620
Deferred tax liabilities:		
Property and equipment	(82)	(48)
Operating lease right-of-use assets	(452)	(572)
Total deferred tax liabilities	(534)	(620)
Net deferred tax assets	$ —	$ —

The provisions of ASC Topic 740, *Accounting for Income Taxes* (ASC 740), require an assessment of both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable. For the years ended December 31, 2022 and 2021, based on all available objective evidence, including the existence of cumulative losses,

the Company determined that it was not more likely than not that the net deferred tax assets were fully realizable. Accordingly, the Company established a full valuation allowance against its deferred tax assets. The Company intends to maintain a full valuation allowance on net deferred tax assets until sufficient positive evidence exists to support reversal of the valuation allowance. The Company's valuation allowance increased by $17.7 million during the year ended December 31, 2022, primarily because of an increase to the Company's net operating losses, credits, stock compensation, and the capitalization of research and development expenses. The Company's valuation allowance increased by $9.4 million during the year ended December 31, 2021, primarily because of an increase to the Company's net operating loss deferred tax assets, credits and intangible deferred tax assets.

At December 31, 2022, the Company had net operating loss carryforwards available to reduce future taxable income, if any, for federal and state income tax purposes of approximately $57.2 million and $1.3 million, respectively. The federal net operating loss carryforwards at December 31, 2022 can be carried forward indefinitely, subject to an annual limitation of 80% of taxable income. The state net operating loss carryforward begins expiring in 2040.

At December 31, 2022, the Company also had federal and California research and development tax credit carryforwards of $1.3 million and $1.1 million, respectively, available to offset future income tax, if any. The federal credit carryforwards begins expiring in 2040, and the California credits can be carried forward indefinitely.

Under Section 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change attributes, such as research tax credits, to offset its post-change income may be limited. In general, an "ownership change" will occur if there is a cumulative change in the Company's ownership by "5-percent shareholders" that exceeds 50 percentage points over a rolling three-year period. Similar rules may apply under state tax laws. Therefore, certain of the Company's carryforward tax attributes may be subject to an annual limitation regarding their utilization against taxable income in future periods. The Company has performed a Section 382 study and has concluded that ownership changes have occurred. As a result, the federal and state NOL carryforwards and tax credit carryforwards maybe subject to annual limitations before being applied to reduce future income tax liabilities.

Uncertain Tax Positions

The Company adopted the provisions of ASC 740, which requires companies to determine whether it is "more likely than not" that a tax position will be sustained upon examination by the appropriate taxing authorities before any tax benefit can be recorded in the financial statements. It also provides guidance on the recognition, measurement, classification and interest and penalties related to uncertain tax positions.

The following table summarizes the activity related to the Company's gross unrecognized tax benefits (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Beginning balance	$ 112	$ —	$ —
Increases for tax provisions related to prior year	133	1	—
Increases for tax provisions related to current year	379	111	—
Ending balance	$ 624	$ 112	$ —

The unrecognized tax benefits, if recognized, would not affect the effective income tax rate due to the valuation allowance that currently offsets deferred tax assets. Interest and penalties were zero. The Company does not expect the unrecognized tax benefits to change significantly over the next twelve months.

The Company files federal and state income tax returns. All periods since inception are subject to examination by federal and state authorities, where applicable. There are currently no pending income tax examinations.

Note 8. Commitments and Contingencies

Operating Leases

The Company leases its headquarters with its main offices and laboratory facilities in Redwood City and San Carlos, California.

In September 2022, the Company entered into a thirty-month sub-lease agreement for office space located at 900 Middlefield Road, 4th Floor, Redwood City, California, which commenced in January 2023 and expires in July 2025. In connection with the sub-lease, the Company made a security deposit of $2.1 million which is included in other assets on the balance sheet at

December 31, 2022. Total future rent payments under the agreement amount to approximately $6.8 million. The Company has not recognized a right-of-use asset or aggregate lease liability as of December 31, 2022 for this lease as the Company did not control the underlying assets at any time during the year ended December 31, 2022.

In November 2021, the Company entered into a four-year lease for additional lab space located at 1585 Industrial Road, San Carlos, California which is expected to commence during the first quarter of 2023. Total future rent payments under the agreement amount to approximately $2.2 million. The Company has not recognized a right-of-use asset or aggregate lease liability as of December 31, 2022 for this lease as the Company did not control the underlying assets at any time during the year ended December 31, 2022.

In September 2021, the Company entered into a sub-lease agreement for additional office space located at 900 Middlefield Road, 4th Floor, Redwood City, California, which commenced in January 2022 and expires in December 2022. In connection with the sub-lease, the Company made a security deposit of $1.1 million which is included in prepaid expenses and other current assets on the balance sheet at December 31, 2022. The Company has elected to apply the short-term lease exception in accordance with ASC 842.

In March 2021, the Company entered into a five-year lease for new lab space located at 1599 Industrial Road, San Carlos, California, which commenced on May 1, 2021 and expires in April 2026. The lease was accounted for under ASC 842. Upon initiation, the Company recognized a right-of-use asset and liability of $3.2 million, discounted at 5.4%, the Company's estimated incremental borrowing rate over the five-year expected remaining term. As of December 31, 2022, the weighted-average remaining lease term is 3.3 years and the weighted-average discount rate is 5.4%.

In February 2021, the Company entered into an eight-month sub-lease agreement for additional office space located at 650 Main Street, Redwood City, California. In September 2021, the Company renewed the lease agreement on a month-to-month basis and the lease ended in January 2022. The Company has elected to apply the short-term lease exception in accordance with ASC 842.

Cash paid for amounts included in the measurement of lease liabilities for the years ended December 31, 2022 and 2021 was $0.7 million and $0.3 million, respectively.

Lease expense was $4.0 million, $1.3 million and $0.2 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Maturities of lease liabilities as of December 31, 2022 were as follows (in thousands):

Year Ending December 31,	Operating Lease Commitments
2023	$ 727
2024	748
2025	771
2026	259
Total undiscounted lease payments	2,505
Less: Present value adjustments	(220)
Total operating lease liabilities	$ 2,285
Operating lease liabilities, current	618
Operating lease liabilities, non-current	1,667
Total operating lease liabilities	$ 2,285

Legal Proceedings

The Company, from time to time, may be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings during the years ended December 31, 2022 and 2021, and, to the best of its knowledge, no material legal proceedings are currently pending or threatened.

Indemnification

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to these arrangements, the Company indemnifies, holds harmless and agrees to reimburse the indemnified parties for losses suffered or incurred by the indemnified party, in connection with any trade secret, copyright, patent or other intellectual property infringement claim by any third party with respect to its technology. The term of these indemnification agreements is generally perpetual any time after the execution of the agreement. The maximum potential amount of future payments the

Company could be required to make under these arrangements is not determinable. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. As a result, the Company believes the fair value of these agreements is not material.

The Company has also entered into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by Delaware corporate law. The Company currently has directors' and officers' insurance.

Note 9. Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share (in thousands except share and per share data):

	Year Ended December 31,		
	2022	2021	2020
Numerator:			
Net loss	$ (81,828)	$ (41,567)	$ (5,324)
Denominator:			
Weighted-average common shares outstanding, basic and diluted	29,271,777	23,858,552	10,532,942
Net loss per share, basic and diluted	$ (2.80)	$ (1.74)	$ (0.51)

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all common stock equivalents outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	December 31,		
	2022	2021	2020
Series A convertible preferred stock	—	—	7,064,925
Stock options, issued and outstanding	5,341,975	4,254,504	—
Estimated shares issuable under the employee stock purchase plan	17,655	6,542	—
Restricted stock, issued and outstanding	292,236	493,914	749,835
Total	5,651,866	4,754,960	7,814,760

Note 10. Selected Quarterly Financial Data (Unaudited)

The following tables provide the selected quarterly financial data for the years ended December 31, 2022 and 2021 (in thousands, except share and per share data):

	2022			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 11,350	$ 12,582	$ 18,242	$ 20,539
General and administrative	5,050	4,892	5,242	5,737
Total operating expenses	16,400	17,474	23,484	26,276
Loss from operations	(16,400)	(17,474)	(23,484)	(26,276)
Interest and other income, net	34	216	594	962
Net loss	$ (16,366)	$ (17,258)	$ (22,890)	$ (25,314)
Net loss per share, basic and diluted	$ (0.56)	$ (0.59)	$ (0.78)	$ (0.86)
Weighted-average number of shares outstanding, basic and diluted	29,126,088	29,196,398	29,319,042	29,441,596

	2021			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 3,798	$ 5,224	$ 7,886	$ 11,088
General and administrative	2,059	3,211	4,752	3,649
Total operating expenses	5,857	8,435	12,638	14,737
Loss from operations	(5,857)	(8,435)	(12,638)	(14,737)
Interest and other income, net	5	36	32	27
Net loss	$ (5,852)	$ (8,399)	$ (12,606)	$ (14,710)
Net loss per share, basic and diluted	$ (0.49)	$ (0.33)	$ (0.43)	$ (0.51)
Weighted-average number of shares outstanding, basic and diluted	11,964,205	25,161,038	29,001,213	29,061,076

Note 11. Subsequent Events

None.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, under the supervision and with the participation of our Chief Executive Officer and our Chief Financial Officer, our principal executive officer and principal financial officer, respectively, conducted an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that as of such date our disclosure controls and procedures were effective at a reasonable assurance level (a) to ensure that information that we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms and (b) to ensure that information required to be disclosed by us in reports filed or submitted under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company's board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company's assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of the company's management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013 framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to our status as an emerging growth company under the JOBS Act.

Changes in Internal Control over Financial Reporting

There were no other changes in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act during the quarter ended December 31, 2022, that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer and principal financial and accounting officer, or persons performing similar functions. A current copy of the code is posted on the Governance section of our website, which is located at investors.biomeafusion.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for our principal executive officer, principal financial and accounting officer, principal accounting officer, or persons performing similar functions, or any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 14. Principal Accountant Fees and Services

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) List the following documents filed as a part of the report:

1. Financial Statements

   The financial statements filed as part of this Annual Report on Form 10-K are listed in the "Index to Financial Statements" under Part II, Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

   Financial statement schedules have been omitted in this Annual Report on Form 10-K because they are not applicable, not required under the instructions, or the information requested is set forth in the financial statements or related notes thereto.

3. Exhibits

   The list of exhibits filed with this Annual Report on Form 10-K is set forth in the Exhibit Index preceding the signature page and is incorporated herein by reference or filed with this Annual Report on Form 10-K, in each case as indicated therein (numbered in accordance with Item 601 of Regulation S-K).

Item 16. Form 10-K Summary

None.

Exhibit Index

Exhibit Number	Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation, as currently in effect	8-K	4/20/2021	3.2	
3.2	Amended and Restated Bylaws, as currently in effect	8-K	4/20/2021	3.4	
4.1	Form of Common Stock Certificate	S-1/A	4/12/2021	4.2	
4.2	Description of Registrant's Securities Registered pursuant to Section 12 of the Securities Exchange Act of 1934	10-Q	5/27/2021	4.4	
4.3	Investors' Rights Agreement, dated December 18, 2020, by and among the Registrant and the investors listed therein	S-1	3/26/2021	10.1	
10.1	Secondary Sublease, dated August 18, 2020, by and between the Registrant and Interactive Memories, Inc. d/b/a Mixbook	S-1/A	4/12/2021	10.2	
10.2	Form of Indemnification and Advancement Agreement for Directors and Officers	10-Q	5/16/2022	10.1	
10.3	Sublease Agreement between the Registrant and Box, Inc., dated September 7, 2022	8-K	9/9/2022	10.1	
10.4	Equity Distribution Agreement, dated November 25, 2022, by and between the Company and Piper Sandler & Co.	8-K	11/25/2022	1.1	

10.5(a)#	Form Executive Change in Control and Severance Agreement	S-1/A	4/12/2021	10.11	
10.5(b)#	Form of First Amendment to Change in Control and Severance Agreement	8-K	4/22/2022	99.1	
10.6(a)#	2020 Equity Incentive Plan	S-1	3/26/2021	10.3(a)	
10.6(b)#	Form of Stock Option Agreement under 2020 Equity Incentive Plan	S-1	3/26/2021	10.3(b)	
10.7(a)#	2021 Incentive Award Plan	S-1/A	4/12/2021	10.4(a)	
10.7(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2021 Incentive Award Plan	S-1/A	4/12/2021	10.4(b)	
10.7(c)#	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2021 Incentive Award Plan	S-1/A	4/12/2021	10.4(c)	
10.7(d)#	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2021 Incentive Award Plan	S-1/A	4/12/2021	10.4(d)	
10.8#	Employee Stock Purchase Plan	S-1/A	4/12/2021	10.5	
10.9#	Employment Offer Letter Agreement by and between the Registrant and Thomas Butler	S-1	3/26/2021	10.6	
10.10#	Employment Offer Letter Agreement by and between the Registrant and Ramses Erdtmann	S-1	3/26/2021	10.7	
10.11#	Employment Offer Letter Agreement by and between the Registrant and Franco Valle	10-Q	8/11/2021	10.2	
21.1	Subsidiaries of the Registrant				X
23.1	Consent of Independent Registered Public Accounting Firm				X
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K)				X
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X

32.2*	Certification of Principal Financial Officer Pursuant o 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

# Indicates a management compensation plan, contract or arrangement

* The certifications attached as Exhibit 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the SEC and are not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Biomea Fusion, Inc.

Date: March 28, 2023 By: /s/ Thomas Butler
Chief Executive Officer
(Principal Executive Officer)

Date: March 28, 2023 By: /s/ Franco Valle
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Thomas Butler and Franco Valle and each of them as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming that said attorneys-in-fact and agents, or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Thomas Butler Thomas Butler	Chief Executive Officer and Director (Principal Executive Officer	March 28, 2023
/s/ Franco Valle Franco Valle	Chief Financial Officer (Principal Financial and Accounting Officer)	March 28, 2023
/s/ Eric Aguiar, M.D. Eric Aguiar, M.D.	Director	March 28, 2023
/s/ Bihua Chen Bihua Chen	Director	March 28, 2023
/s/ Rainer Erdtmann Rainer Erdtmann	Director	March 28, 2023
/s/ Michael J. M. Hitchcock, Ph.D. Michael J. M. Hitchcock, Ph.D.	Director	March 28, 2023
/s/ Sumita Ray, J.D. Sumita Ray, J.D.	Director	March 28, 2023
/s/ Elizabeth Faust, Ph.D. Elizabeth Faust, Ph.D.	Director	March 28, 2023

WE AIM TO CURE

- Thomas Butler, CEO & Chairman

CORPORATE INFORMATION

Executive Management

Thomas Butler
Chief Executive Officer

Ramses Erdtmann
President and Chief Operating Officer

Heow Tan
Chief Technical and Quality Officer

Naomi Cretcher
Chief People Officer

Franco Valle
Chief Financial Officer

Steve Morris, M.D.
Chief Medical Officer

Board of Directors

Thomas Butler
Chairman

Eric Aguiar, M.D.
Lead Director

Ramses Erdtmann
Director

Bihua Chen
Director

Michael J.M. Hitchcock, Ph.D.
Director

Sumita Ray, J.D.
Director

Elizabeth Faust, Ph.D.
Director

Corporate Headquarters

900 Middlefield Road, 4th Floor
Redwood City, CA, 94063

Investor Relations Contact

Chunyi Zhao, Ph.D.
czhao@biomeafusion.com

Corporate Counsel

Goodwin Procter LLP
San Francisco, CA

Transfer Agent

American Stock Transfer
& Trust Company, LLC
Brooklyn, New York
(800) 937-5449

Independent Registered Public Accounting Firm

Deloitte & Touche LLP
San Francisco, CA

The letter to shareholders along with the Form 10-K in this Annual Report contains certain forward-looking statements that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. Such forward-looking statements include statements regarding, among other things, the clinical and therapeutic potential of BMF-219 and BMF-500 and other product candidates that we may identify and advance, progress and expected timing of Biomea Fusion's research and development programs and clinical trials and plans regarding future IND submissions, clinical trials and development activities, including additional indications that we may pursue. Factors that may cause actual results to differ materially include the risk that compounds that appear promising in early research or clinical trials do not demonstrate safety and/or efficacy in later preclinical studies or clinical trials, the risk that Biomea Fusion may not obtain approval to market its product candidates, uncertainties associated with performing clinical trials, regulatory flings and applications, risks associated with reliance on third parties to successfully conduct clinical trials, the risks associated with reliance on outside financing to meet capital requirements, and other risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. You are urged to consider statements that include the words "may," "will," "would," "could," "should," "believes," "estimates," "projects," "promise," "potential," "expects," "plans," "anticipated," "intends," "continues," "designed," "goal," or the negative of those words or other comparable words to be uncertain and forward-looking. For a further list and description of the risks and uncertainties the company faces, please refer to the company's periodic and other filings with the Securities and Exchange Commission, which are available at www.sec.gov. Such forward-looking statements are current only as of the date they are made, and Biomea Fusion assumes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

OUR MISSION IS TO REVOLUTIONIZE MEDICINE BY CREATING THERAPIES THAT CURE PATIENTS OF THEIR DISEASE

We leverage our drug design and operational expertise to create novel covalent small molecules to treat serious and life-threatening diseases. All our molecules are invented and created in-house. They are highly selective, targeted medicines, that address key mechanisms of our patient's disease progression. We have built an R&D engine that has so far produced three novel, covalent inhibitor programs that are currently in preclinical and clinical development. Our team is engaged in all phases of drug discovery and development, including target selection, small molecule design, and preclinical and clinical studies to develop our innovative medicines.

biomea FUSION

Corporate Headquarters
900 Middlefield Road, 4th Floor
Redwood City, CA, 94063