Table of Contents

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 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 001-38410

BioXcel Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**82-1386754**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
555 Long Wharf Drive	**06511**
New Haven CT	(Zip Code)
(Address of principal executive offices)	

Registrant's telephone number, including area code: **(475) 238-6837**

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

Title of each class	Trading Symbol(s)	Name of exchange on which registered
Common Stock, par value $0.001 per share	**BTAI**	**Nasdaq Capital 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 Section 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, a 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 Act). Yes ☐ No ☒

As of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $250,888,981 (based upon the closing sale price of the registrant's common stock reported on the Nasdaq Capital Market on that date). This calculation excludes shares held by the registrant's current directors and executive officers and stockholders that the registrant has concluded are affiliates of the registrant.

There were 29,009,536 shares of our common stock outstanding at March 13, 2023.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2023 annual meeting of stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2022, are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The words "anticipate," "believe," "can," "continue," "could," "designed," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. All statements contained in this Annual Report on Form 10-K, other than statements of historical fact, are forward-looking statements, including, without limitation, statements regarding:

- our ongoing commercialization plans for IGALMI™;
- our plans relating to clinical trials for our product candidates;
- our plans to research, develop and commercialize our current and future product candidates;
- our plans to seek to enter into collaborations for the development and commercialization of certain product candidates;
- the potential benefits of any future collaboration;
- the timing of and our ability to obtain and maintain regulatory approvals, including 505(b)(2) regulatory approval, for our product candidates;
- the rate and degree of market acceptance, clinical utility, number of prescribers and formulary wins of IGALMI and any product candidates for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy, including the potential benefits from any advertising campaigns;
- our participation in, and any potential benefits from, events, conferences, presentations and conventions;
- our intellectual property position and strategy;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing;
- potential investments in, or other strategic options for, our subsidiary, OnkosXcel Therapeutics, LLC;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations; and
- our relationship with BioXcel LLC.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, those listed under Part I, Item 1A. "Risk Factors," Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report on Form 10-K. These and other important factors discussed under the caption "Risk Factors" in our other filings with the Securities and Exchange Commission ("SEC") could cause actual results to differ materially from those indicated by the forward-looking statements made in this filing. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

As used in this Annual Report on Form 10-K, unless otherwise specified or the context otherwise requires, the terms "we," "our," "us," the "Company" or "BTI" refer to BioXcel Therapeutics, Inc., and "BioXcel, LLC" refers to the Company's former parent company and significant stockholder, BioXcel LLC, and its predecessor, BioXcel Corporation. All brand names or trademarks appearing in this Annual Report on Form 10-K are the property of their respective owners, including IGALMI, which is a trademark of BioXcel Therapeutics, Inc.

We may use our website as a distribution channel of material information about the Company. Financial and other important information regarding the Company is routinely posted on and accessible through the Investors & Media section of its website at *www.bioxceltherapeutics.com*. In addition, you may automatically receive email alerts and other information about the Company when you enroll your email address by visiting the "Email Alerts" option under the News / Events menu of the Investors & Media section of our website at *www.bioxceltherapeutics.com*.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. "Risk Factors" in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- We have a limited operating history and have not generated substantial product revenues to date, which may make it difficult to evaluate the success of our business to date and to assess our future viability.
- We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.
- We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We have significant indebtedness and other contractual obligations that could impair our liquidity, restrict our ability to do business and thereby harm our business, results of operations and financial condition. We may not have sufficient cash flow from operations to satisfy our obligations under our financing facilities.
- We have limited experience in drug discovery and drug development.
- In the near term, we are dependent on the success of IGALMI, and three of our product candidates, BXCL501, BXCL502 and BXCL701. If we are unable to complete the clinical development of or obtain marketing approval for our product candidates or successfully commercialize IGALMI or our product candidates, either alone or with a collaborator, or if we experience significant delays in doing so, our business could be substantially harmed.
- 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.
- The regulatory approval processes of the United States ("U.S.") Food and Drug Administration ("FDA"), and comparable foreign authorities, are lengthy, time consuming, expensive and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.
- Clinical trials are expensive, time-consuming, and difficult to design and implement, and involve an uncertain outcome.
- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval.

- BioXcel LLC's approach to the discovery and development of product candidates based on EvolverAI, its proprietary pharmaceutical discovery and development engine, is novel and unproven, and we do not know whether we will be able to develop any products of commercial value.
- If we are required by the FDA or similar regulatory authorities to obtain approval (or clearance, or certification) of a companion diagnostic device in connection with approval of one of our product candidates, and we do not obtain or face delays in obtaining approval (or clearance, or certification) of a companion diagnostic device, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.
- Although the FDA approved IGALMI for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder, we still face extensive and ongoing regulatory requirements and obligations for IGALMI and for any product candidates for which we obtain approval.
- The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.
- If our products do not gain market acceptance, our business will suffer because we might not be able to fund future operations.
- If we are unable to develop satisfactory sales and marketing capabilities, we may not succeed in commercializing IGALMI or any product candidate for which we may obtain regulatory approval.
- Although we obtained FDA approval for IGALMI, our products and product candidates may not be accepted by physicians or the medical community in general.
- We continue to depend on BioXcel LLC to provide us with certain services for our business.
- We are substantially dependent on third parties for the manufacture of our clinical supplies of our product candidates, and our commercial supplies of IGALMI, and we intend to rely on third parties to produce commercial supplies of any other approved product candidate. Therefore, our development of our products could be stopped or delayed, and our commercialization of any future product could be stopped or delayed or made less profitable if third-party manufacturers fail to obtain approval of the FDA or comparable regulatory authorities or fail to provide us with drug product in sufficient quantities or at acceptable prices.
- Data breaches or cyber-attacks could disrupt our business operations and information technology systems, and financial results, or result in the loss or exposure of confidential or sensitive Company information.
- We face risks associated with the increased scrutiny relating to environmental, social and governance matters.
- It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection. If our patent position does not adequately protect our product candidates, others could compete against us more directly, which would harm our business, possibly materially.

TRADEMARKS, TRADE NAMES AND SERVICE MARKS

This Annual Report includes our trademarks, trade names and service marks, including, without limitation, "IGALMI™" and our logo, which are our property and are protected under applicable intellectual property laws. Solely for convenience, trademarks, trade names and service marks may appear in this Annual Report without the ®, TM and SM symbols, but such references are not intended to indicate, in any way, that we or the applicable owner forgo or will not assert, to the fullest extent permitted under applicable law, our rights or the rights of any applicable licensors to these trademarks, trade names and service marks. We do not intend our use or display of other parties' trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

INDUSTRY AND OTHER DATA

Unless otherwise indicated, information contained in this Annual Report concerning our industry and the markets in which we operate, including our general expectations, market position and market opportunity, is based on our management's estimates and research, as well as industry and general publications and research, surveys and studies conducted by third parties. We believe the information from these third-party publications, research, surveys and studies included in this Annual Report is reliable. Management's estimates are derived from publicly available information, their knowledge of our industry and their assumptions based on such information and knowledge, which we believe to be reasonable. This data involves a number of assumptions and limitations which are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in this Annual Report under "Forward Looking Statements" and Part I, Item 1A "Risk Factors." These and other factors could cause our future performance to differ materially from our assumptions and estimates.

PART I

Item 1. Business

Overview

BioXcel Therapeutics, Inc. ("BTI" or the "Company") is a biopharmaceutical company utilizing artificial intelligence ("AI") approaches to develop transformative medicines in neuroscience and immuno-oncology. We are focused on utilizing cutting-edge technology and innovative research to develop high-value therapeutics aimed at transforming patients' lives. We employ a proprietary AI platform to reduce therapeutic development costs and potentially accelerate development timelines. Our approach leverages existing approved drugs and/or clinically evaluated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indications. We believe this differentiated approach has the potential to reduce the expense and time associated with drug development in diseases with substantial unmet medical needs.

On April 6, 2022, we announced that the U.S. FDA approved IGALMI (dexmedetomidine or "Dex") sublingual film for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults. IGALMI is approved to be self-administrated by patients under the supervision of a health care provider. We deployed the first phase of our sales team for high priority targets in May 2022. Furthermore, on July 6, 2022, we announced that IGALMI was commercially available in doses of 120 and 180 microgram ("mcg") through the Company's third-party logistics provider and was available for order through wholesalers.

Our most advanced clinical development program is BXCL501, an investigational proprietary, orally dissolving, film formulation of Dex for the treatment of agitation associated with psychiatric and neurological disorders.

We are conducting clinical trials for the at-home use of BXCL501 for agitation associated with bipolar disorders and schizophrenia. We also continue to conduct clinical trials evaluating BXCL501 for the acute treatment of agitation in Alzheimer's disease patients in residential care facilities and nursing homes and for adjunctive treatment of patients with Major Depressive Disorder ("MDD").

Our advanced immuno-oncology asset, BXCL701, is an investigational, oral innate immune activator currently being developed as a potential therapy for the treatment of aggressive forms of prostate cancer, pancreatic cancer, and other solid and liquid tumors.

We continue to work closely with our clinical sites to monitor the potential impact of the evolving COVID-19 pandemic and the spread of its variants. To date, we have not experienced any significant delays in any of our ongoing or planned clinical trials, except for occasional COVID-19 related disruptions to our TRANQUILITY II and PLACIDITY trials. However, this could change rapidly.

Neuroscience

Our Neuroscience Strategy

Our goal is to become the leading AI-enabled neuroscience therapeutics company. We continue to evaluate all strategic options available to us for our neuroscience assets, which could include licensing, partnering, and co-commercialization.

Our Novel Drug Re-Innovation Approach

We aim to develop and implement, holistically throughout the drug development process, an AI ecosystem designed to rapidly identify medications related to our key focus areas of neuroscience and immuno-oncology. Our in-house, uniquely integrated AI-to-drug-development capability is complemented by the services and technology of BioXcel LLC, our former parent company. For example, we have constructed a labeled properties graph (also referred to as a "knowledge graph") that visually relates neuropsychiatric symptoms, brain circuits, drug targets, and existing drugs. By making these connections, new potential uses for existing drugs emerge. The knowledge graph may be queried to uncover not only single drugs but potentially new combinations of drugs that we believe may be more effective in

treating disorders than single agents. New combinations of drugs provide the opportunity to evaluate lower, potentially tolerable doses of drugs, and provide the basis for stronger intellectual property positions. Our AI team works closely with our Business Development team to prioritize the most valuable external opportunities in a data-driven manner. These opportunities may be found in new potential uses for launched drugs, in drugs that are part of pharmaceutical company pipelines no longer being pursued, or within academic efforts to develop new drug candidates.

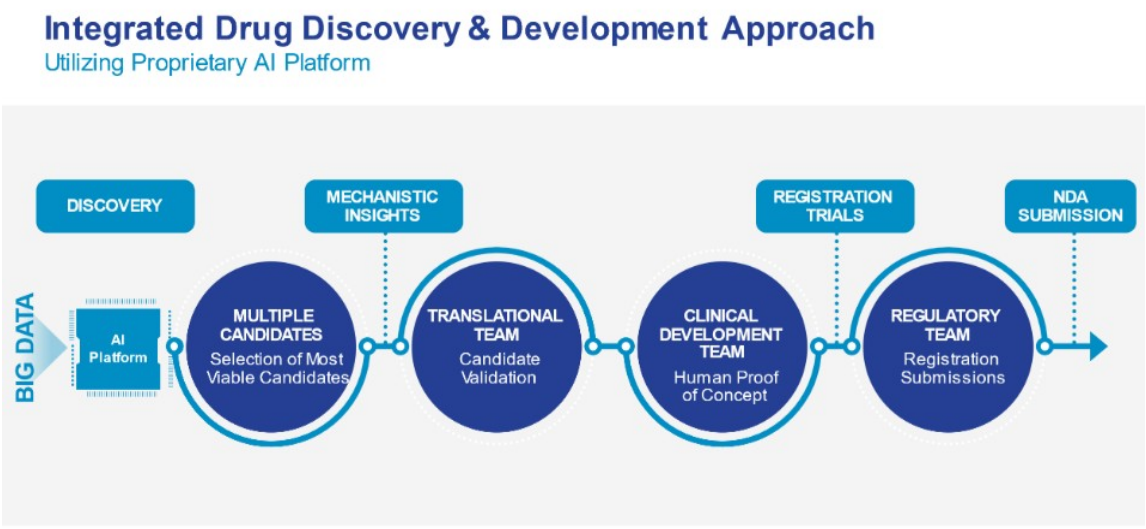
In addition to our AI approach to neuropsychiatric symptoms and neurological rare diseases, in immuno-oncology we are actively examining signaling pathways in tumors that we believe are potential targets for synergistic drug combinations. We believe synergistic drug combinations may allow more effective treatments by reducing the probability of drug adaptation by cancer cells. AI is useful in matching existing oncology drugs and their mechanism of action to specific types of cancer, as well as in identifying combinations that we believe may have a higher probability of success.

Traditional drug development is plagued with low success rates, long drug development cycles, and exorbitant development costs. Furthermore, many serious diseases continue to go unaddressed due to limitations of the current drug discovery paradigm. The pharmacological universe spans more than 27,000 active pharmaceutical agents, but only approximately 4,000 are approved and marketed drugs benefiting patients. These marketed drugs may be applied to other indications, including rare diseases, and represent an untapped potential for meeting significant unmet medical needs and recouping research and development investments. Many of the remaining agents are clinical candidates that are active, shelved, or have failed for reasons other than toxicity and that can potentially be re-engineered for different indications or patient segments. The remaining agents potentially represent an unrealized investment of billions of research and development dollars by the private and public sectors, resulting in an immeasurable amount of patient suffering and sacrifice during clinical development. Also, these compounds usually have known pharmacokinetic properties allowing for a more data-driven selection of appropriate doses for development programs. Finally, with respect to neuropsychiatric indications, we prioritize those compounds with structural design features that may contribute to high blood-brain barrier permeability, which may increase the likelihood of compound penetration into the brain. Lack of brain penetration is a common cause for failure of many drugs developed for neuropsychiatric indications. In addition, BioXcel LLC is prioritizing compounds with available human safety data, acceptable pharmacokinetic results, and data that supports a high probability of achieving reasonable brain concentrations after dosing. The compounds in our pipeline have been identified using this proprietary platform.

This drug re-innovation model has been exemplified by the successful development and commercialization of drugs such as Tecfidera® (Biogen, Inc.), Thalomid® (Celgene Corporation), and Viagra® (Pfizer, Inc.). All of these drugs were identified by insights in biology and disease pathophysiology. The successful business models of biotech companies like Axsome Therapeutics, Inc. and Karuna Therapeutics, Inc. are based on the re-innovation and combination of existing clinical candidates or marketed drugs to provide novel solutions for patients. Unfortunately, such discoveries have been severely limited in scope due to the lack of a genuinely integrated approach to mining big data and advanced analytics.

Our AI-based discovery and development process is the foundation of our drug re-innovation model for identifying the next wave of potential medicines. Our therapeutic area experts have over 200 years of combined experience across the drug discovery and development value chain. We believe that our method of finding potential product candidates gives us a higher probability of success because it combines the comprehensiveness and efficiency of machine learning and big data analytics with the expertise and intuition of human experience in drug development. We believe the combination of AI and drug discovery and development expertise facilitates the generation of therapeutic candidates and gives us a significant competitive advantage.

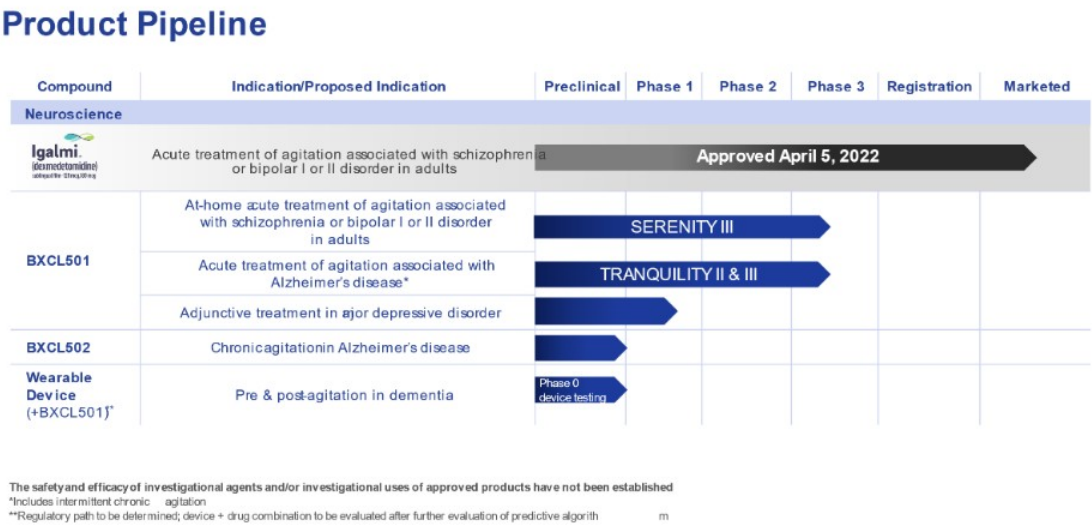
Our approach is illustrated below:



We continue to integrate and evolve our neuroscience and immuno-oncology AI machine learning and drug discovery and development platform. Our platform led to the identification and rapid development of IGALMI, as well as the advancement of other potential indications. We are continuing to leverage our platform to identify and develop new neuroscience and immuno-oncology programs.

Our Neuroscience Programs

The following is a summary of the status of our neuroscience clinical development programs as of the date of this Annual Report on Form 10-K:

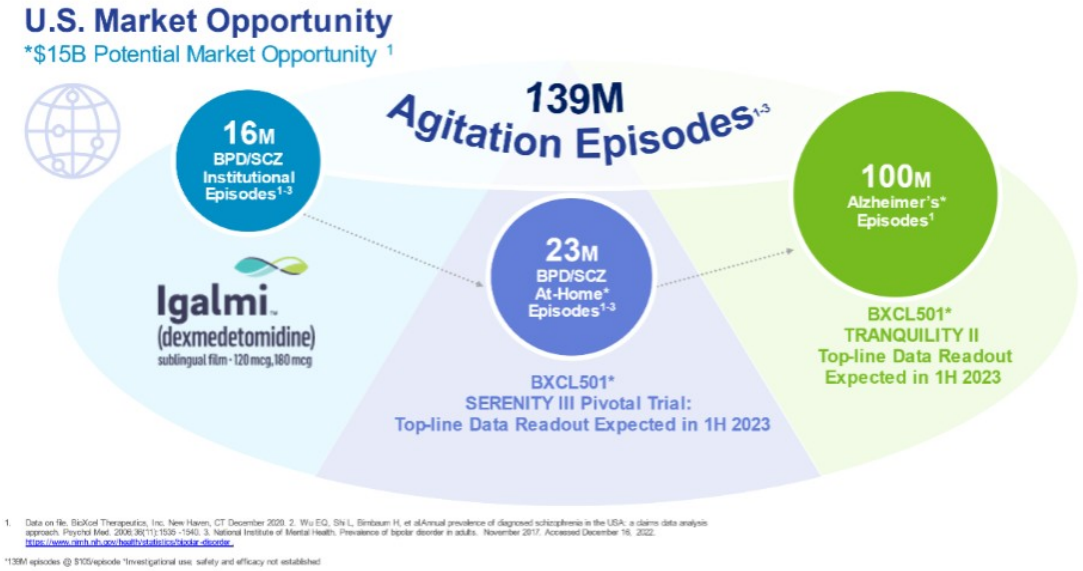


As a selective adrenergic agent with a sublingual or buccal route of administration, BXCL501 is designed to be easy to administer and has shown a rapid onset of action in multiple clinical trials, including clinical trials studying patients with schizophrenia, bipolar disorders, and dementia. We believe the results from these studies suggest that BXCL501 has the potential to generate a calming effect without producing excessive sedation. We believe that BXCL501 is highly differentiated from antipsychotics currently used as a standard of care for the treatment of agitation that often produce unwanted side effects such as excessive sedation and extra-pyramidal motor effects. Managing patient agitation in neuropsychiatric and neurodegenerative disorders represents a significant challenge for physicians and caregivers. We believe that BXCL501 has the potential to address these challenges while providing an efficient treatment regimen for patients.

Agitation Overview and Market Opportunity

Agitation in patients with neuropsychiatric diseases is a serious medical condition. Agitation is characterized by feelings of unease, excessive talking, and/or unintentional and purposeless motions, such as wringing of the hands or pacing. People experiencing agitation may also express excitement, hostility, poor impulse control, tension, uncooperativeness, and occasional disruptive behavior, which may lead to aggression and violence. In many cases, people develop agitation when treatment for their underlying disorder is not working well. Stressful situations or traumatic events can also trigger agitation. Agitation can occur suddenly or slowly and vary in length, lasting for a few minutes or for an extended period.

With the agitation issues associated with schizophrenia and bipolar disease coupled with a fast-growing elderly population that is potentially likely to experience agitation associated with Alzheimer’s disease, the difficulties, and expenses of acute treatment of agitation are expected to grow significantly. Below are estimated statistics associated with annual agitation episodes associated with bipolar disorders, schizophrenia, and Alzheimer’s disease in the U.S.



Treatments for Agitation

Antipsychotics, the current standard of care for acute treatment of agitation in schizophrenia and bipolar disorder, are also used off-label to treat agitation in dementia and other conditions. Side effects of these medications include movement disorders, including akathisia and extrapyramidal symptoms. One of the serious limitations of these drugs is that they can sedate the patient and do not permit verbal interaction with the hospital staff to continue. Intramuscular ("IM")-delivered antipsychotics, such as haloperidol and olanzapine, are used extensively in this setting but are invasive and often require patient restraint. This type of treatment can dehumanize patients and cause trauma that could have long-term impact on them. Furthermore, these treatments include a black box warning for use in elderly patients.

While sublingual tablet formulations utilizing antipsychotics have been developed, these formulations have long half-lives (21-24 hours) and significant side effects when given acutely or chronically. Oral agents such as benzodiazepines are also used but have a slow onset of action and are consequently ineffective in the acute treatment of agitation. Side effects of these agents include sedation, amnesia, confusion, and paradoxical responses. They can intensify cognitive slowing and worsen memory and motor impairment, contributing to an increased risk of falls and fractures. In addition, long-term use of benzodiazepines has been found to be habit-forming and can cause addiction or relapse to abuse substances. Nonadherence with oral agents can also be problematic as patients may attempt to spit out these medications. We believe that, based on the current method of administration of oral medicine for agitation, the orally dissolving, mucoadhesive film offers compliance advantages as it will more likely prevent patients from avoiding treatment.

The sublingual or buccal route of administration is an accepted alternative to oral administration of drug delivery to the central nervous system when rapid onset or more controlled delivery is required. Currently, there are six products approved for film administration, including our product, IGALMI. For example, BioDelivery Sciences International, Inc., a commercial-stage specialty pharmaceutical company dedicated to patients living with chronic conditions, has developed a buccal film formulation of buprenorphine for chronic pain management and buprenorphine and naloxone for opioid dependence. We developed BXCL501 as a differentiated sublingual film dosage form of Dex, which we believe may offer benefits such as ease of use and quick absorption for rapid therapeutic effects.

Mechanism of Action: α2a Adrenergic Receptor and NE Role in Acute Agitation

BXCL501 is designed to be easily administered and have a rapid onset of action. We believe that BXCL501, with its differentiated pharmacology and ease of administration, could potentially be a first-in-class, non-invasive acute treatment for agitation that can be rapidly administered by physicians and caregivers. Dex is approved in the U.S. for the sedation of initially intubated and mechanically ventilated patients during treatment in the intensive care unit ("ICU"). It is also used in the intensive care setting for sedation of non-intubated patients prior to and/or during surgical and other invasive procedures. Dex, launched in the U.S. as Precedex™ in 1999, is a selective α2a adrenergic receptor agonist that has a strong safety record and has been studied in over 130 clinical trials to date. It has also been sold in the European Union ("EU") and other countries under the trade name Dexdor® as a sedative for intensive care patients. Dex was approved by the European Commission for sedation of adult ICU patients requiring a sedation level no deeper than arousal in response to verbal stimulation (corresponding to Richmond Agitation-Sedation Scale 0 to -3). It has been used to prevent or treat hyperactive delirium resulting from anesthesia in the ICU. Given these uses of the IV formulation of Dex, we believe Dex formulated in a sublingual film and at much lower doses will allow for ease of administration in settings where rapid acute treatment of agitation is needed.

IGALMI Commercial Progress

Since the commercial launch of IGALMI in July 2022, our commercial progress has yielded more than 65 formulary wins. Additionally, more than 600 hospital pharmacy and therapeutics ("P&T") committees are scheduled to review and vote on IGALMI inclusion in their formularies over the next several months. In addition, nearly 50% of target beds are now under group purchasing organization ("GPO") contracts as of February 28, 2023. We are in active discussions with other leading GPOs. This has been primarily accomplished with our initial 26-person institutional sales force since our trade launch in July 2022.

We expanded our institutional sales force to 70 representatives in December 2022 to cover over 1,700 target hospitals as of February 28, 2023. During the fourth quarter of 2022, our Corporate Account Director team was focused on 59 high-volume, high-control integrated delivery network ("IDN") accounts. Formulary voting is currently scheduled for approximately 70,000 (25%) of our target IDN beds, with approximately 7,000 (2%) now approved.

We believe the value proposition for IGALMI will continue to evolve as we learn from market response. Staff shortages in the emergency departments ("EDs") of hospitals, complicated by the potential for staff injuries due to agitated patients, are becoming increasingly concerning to hospital administration. Due to limited agitation treatment options in the ED, IM injection is often used. This approach can be both confrontational and coercive to agitated patients, often making their symptoms worse. Moreover, these patients may occupy ED beds for extended periods due to unresponsive sedation, reducing throughput and increasing costs. These conditions continue to reinforce the need for a drug with IGALMI's profile.

We are seeing our marketing efforts continue to drive awareness through an extensive convention presence, peer influence programs, and digital marketing campaigns. As of December 31, 2022, our peer-led IGALMI speaker programs have educated over 1,000 health care providers, while we have had over 350,000 web sessions on our branded health care provider website and additional touchpoints through other digital marketing efforts. With our sales team expansion and as we begin to garner additional P&T formulary adoption, we plan extensive digital and peer-to-peer marketing efforts in the first half of 2023 to continue to raise awareness, reinforce key messages, and drive additional demand. In addition, we have planned promotional presence at leading national and regional conferences in 2023.

If IGALMI is approved outside the U.S., we would consider launching the product through collaborations with third parties.

Our continued commercialization efforts for IGALMI are designed to build the foundation to launch additional potential follow-on indications, if any, paving the way for our expanding neuroscience business.

BXCL501 Development

In indications other than approved by the FDA as IGALMI, BXCL501 remains an investigational, proprietary, orally dissolving film formulation of Dex, a selective alpha-2 receptor agonist, targeting symptoms from stress-related

behaviors such as agitation. BXCL501 is our most advanced neuroscience clinical program, being evaluated for at-home acute treatment of agitation related to schizophrenia and bipolar disorders, the acute treatment of agitation related to Alzheimer's disease, and as an adjunctive treatment for MDD in conjunction with the use of Selective Serotonin Reuptake Inhibitors ("SSRIs") or Serotonin Norepinephrine Reuptake Inhibitors ("SNRIs") alone.

As a selective adrenergic agent with a sublingual or buccal route of administration, BXCL501 is designed to be easily administered and has shown a rapid onset of action in multiple clinical trials, including clinical trials studying patients with schizophrenia, bipolar disorders, and Alzheimer's disease. We believe results from these studies suggest that BXCL501 has the potential to reduce agitation without producing excessive sedation. We also believe BXCL501 is highly differentiated from antipsychotics, which often produce unwanted side effects such as excessive sedation or extrapyramidal motor effects, currently used as a standard of care to treat agitation. Managing patient agitation in neuropsychiatric and neurodegenerative disorders represents a significant challenge for physicians and caregivers. We believe BXCL501 has the potential to address these challenges while providing an efficient treatment regimen for patients.

We also believe that BXCL501, if approved for the respective indications, has the potential to become the standard of care for the acute treatment of agitation arising from diseases such as schizophrenia and bipolar disorder (SERENITY I and II trials); and Alzheimer's disease (TRANQUILITY II and TRANQUILITY III trials within our pivotal Phase 3 program).

In addition, given the differentiated design of BXCL501 and its potential mechanism of action, we believe BXCL501 has the potential to address several diseases or conditions for which agitation is a symptom of the condition or underlying disease, including as an adjunctive treatment for MDD, opioid withdrawal (RELEASE trial), and post-traumatic stress disorder ("PTSD").

BXCL501 Clinical Trials

TRANQUILITY Program

The TRANQUILITY I study of agitation in dementia concluded with a total of 46 subjects in Part B testing the 40mcg dose versus placebo. The purpose of enrolling this additional cohort was to gather additional evidence supporting dose selection and to provide data for statistical powering of large multiple-site Phase 3 pivotal trials. All patients were able to take the film themselves and properly place it. There were no serious adverse events ("SAEs") related to the drug, and no falls, loss of consciousness, or syncopal events reported. There were also no local tolerability issues. The adverse events ("AEs") observed for 40mcg were consistent with those previously observed for 30mcg, 60mcg, and placebo doses. The incidence of individual and categorical AEs for the 40mcg dose were lower than the 60mcg group, and similar to the 30mcg dose group.

Efficacy was measured by the change from pre-dose baseline Positive and Negative Syndrome Scale Excitatory Component ("PEC") total score at two hours, the same primary endpoint utilized in prior pivotal trials of BXCL501. The 40mcg dose showed statistically significant reductions in PEC total score at two hours and demonstrated statistically significant separation from placebo as early as one hour. The magnitude of change in PEC total score was statistically greater for the 40mcg dose than that of 30mcg and somewhat less than the 60mcg dose in previous cohorts. Overall, we believe the 40mcg data support continued evaluation of both 40mcg and 60mcg doses in Phase 3 pivotal trials.

On December 15, 2021, after our initial Breakthrough Therapy designation meetings with the FDA, we announced the initiation of our program to evaluate BXCL501 for the treatment of acute agitation associated with Alzheimer's disease. The program's two studies, TRANQUILITY II and TRANQUILITY III, are designed to evaluate the safety and efficacy of BXCL501 in adults 65 years and older across the range of illness including mild, moderate, and severe dementia in assisted living or residential facilities and nursing homes. Patient enrollment is complete for TRANQUILITY II.

- The program consists of two randomized, double-blind, placebo-controlled, adaptive, parallel group pivotal trials: TRANQUILITY II and TRANQUILITY III.

- Each study will enroll approximately 150 dementia patients 65 years and older. Patients will self-administer 40mcg or 60mcg of BXCL501 or placebo whenever agitation episodes may occur.

- TRANQUILITY II enrolled patients with mild to moderately severe dementia in assisted living or residential care facilities who generally require minimal assistance with activities of daily living. Enrollment is complete and nearing completion of a three-month observation period. We expect to announce top-line data in the second quarter of 2023.

- TRANQUILITY III enrolled patients with moderate to severe dementia who require moderate or greater assistance with activities of daily living. This study initiated with the first patient dosed in December 2022.

- The studies are designed to assess agitation as measured by the changes from baseline in the PEC total score and total Pittsburgh Agitation Scale scores. For both studies, the primary efficacy endpoint will be the change in PEC total score from baseline measured at two hours after the initial dose.

- Patients who complete TRANQUILITY II or TRANQUILITY III will be eligible to enroll in an open label, 52-week safety study designed to describe the safety of BXCL501 in continued use. This study is expected to initiate in the second half of 2023.

Bipolar or Schizophrenia-related Agitation (At-Home Use)

We met with the FDA in July 2022 to discuss the design of a registrational study to support potential expansion of BXCL501's approved indication to enable at-home use for the acute treatment of agitation related to schizophrenia and bipolar disorders. We believe we reached alignment with the FDA on key design features with respect to our SERENITY III study, which consists of two parts. The first part is comparable to the pivotal SERENITY I and II studies. Using similar inclusion and exclusion criterion in an inpatient setting, acutely agitated patients with schizophrenia or bipolar disorders will be randomized to self-administer either 60mcg of BXCL501 or placebo in a double-blind placebo-controlled trial. The primary endpoint of Part 1 of the study is the PEC total score change from baseline at two hours post-dose. The secondary objective is to assess safety and tolerability. The first part of SERENITY III initiated with the first patients dosed in December 2022. Part 1 enrollment was completed in March 2023, with top-line efficacy results also expected in the second quarter of 2023. Part 2 of the study is expected to initiate in the second quarter of 2023. The primary objective is to assess the safety of a 60mcg dose when self-administered in an at-home setting. Patients with schizophrenia or bipolar disorders and a history of agitation will be randomized to self-administer 60mcg of BXCL501, or placebo, when they may experience an episode of acute agitation at-home over a period of three months. Patients will return for regularly scheduled outpatient visits where investigators will review information collected from patients and reliable informants to determine and characterize any adverse effects.

Major Depressive Disorder

We expanded our development pipeline to evaluate BXCL501 as a potential adjunctive treatment for MDD. The initial clinical study in this program is a double-blind, placebo-controlled, multiple ascending dose trial designed to evaluate the safety and tolerability of daily doses of BXCL501 in healthy volunteers. We expect to report top-line results in the second quarter of 2023. As of February 28, 2023, seven dosing cohorts of healthy adult volunteers have been completed, including cohorts receiving 30mcg, 60mcg, 80mcg, or 120mcg BXCL501 (or placebo) once daily for seven days, and with cohorts receiving twice-a-day dosing of 30mcg in the morning and 60mcg in the evening (or placebo). A cohort of subjects received 40mcg in the morning and 80mcg in the evening (or placebo). The final cohort tested 60mcg in the morning and 80mcg in the evening (or placebo) plus twice daily 30 milligrams ("mg") duloxetine in the morning and evening. BXCL501 has been generally well tolerated across completed cohorts. We anticipate that the safety and tolerability results of this study will enable dose selection for a Phase 2 proof-of-confidence trial in MDD.

Pediatric Study

In June 2021, we initiated a global clinical trial designed to evaluate the safety and efficacy of BXCL501 in the acute treatment of agitation associated with pediatric schizophrenia and bipolar disorders, in part to fulfill pediatric study requirements agreed to with the FDA in connection with IGALMI's approval. The trial protocol has been reviewed by

the FDA, as well as by the European Medicines Agency ("EMA"), to fulfill potential commitments to study the effects of BXCL501 in pediatric patients ages 13-17 with schizophrenia and ages 10-17 with bipolar disorders. Enrollment of patients with schizophrenia, schizoaffective disorder, bipolar I, and bipolar II disorder is ongoing in this multisite, double-blind, placebo-controlled parallel group trial. Approximately 40% of the 150 total subjects have been enrolled in the U.S. and several European sites are planned to initiate enrollment in the second quarter of 2023. Similar to our registration trials in schizophrenia and bipolar disorder (SERENITY I and II), the primary endpoint is the change from baseline PEC total score at two hours.

Additional Neuroscience Opportunities

BXCL501 Pipeline Opportunities for Franchise Expansion

Given the differentiated design of BXCL501 and its selective mechanism of action, we believe BXCL501 has the potential for broad applicability across several indications where agitation is a symptom of a condition or underlying disease.

The Pharmacotherapies for Alcohol and Substance Use Disorders Alliance ("PASA") is funded by the Congressionally Directed Medical Research Programs as part of its Alcohol and Substance Use Disorder Research Program. The goal of PASA is to fund research for developing new medications that can improve treatment outcomes for alcohol and substance use disorders; especially as related to post-traumatic stress disorder ("PTSD") and other psychological disorders. In December 2020, the Veterans Affairs Connecticut Healthcare System and Yale University Medical School were awarded a grant by PASA to evaluate BXCL501 in patients with PTSD who suffer from alcohol use disorder ("AUD"). This study is currently underway and the Company is providing BXCL501 for the study to evaluate whether BXCL501 has the potential to treat AUD in this patient population.

As announced on August 1, 2022, the National Institutes of Health ("NIH") National Institute on Drug Abuse awarded a grant to Columbia University, as part of the NIH's Helping to End Addiction Long-term ("HEAL") initiative, to fund clinical testing of BXCL501 as a potential treatment for opioid withdrawal. The goal of the NIH HEAL Initiative program is to support preclinical and clinical research studies that will have high impact and quickly yield the necessary results to advance medications closer to FDA approval to prevent and treat opioid use disorder and overdose. The Company will supply the drug product for the conduct of this multi-site study; the first patient was recently dosed in this study, which is expected to be completed in 2024.

We are currently conducting studies designed to develop algorithms for wearable technologies that are designed to detect early signs of agitation. We completed a study in October 2022 using wearable technologies (i.e., smart watches and phones) in an effort to detect signals related to agitation in healthy subjects that were administered Yohimbine, a compound that can elicit a mild hyper-arousal in humans; hyper-arousal is related to agitation. Data from this study were analyzed and identified a robust signal that differentiated Yohimbine-treated subjects from those that received a placebo. We plan to utilize the data from this study to train an algorithm to predict emergence of agitation in patients, which we believe, if successful, may allow for early treatment and prevention of agitation.

BXCL502 Development

We identified a second neuropsychiatric drug candidate, BXCL502, through our AI-based platform. We plan to evaluate BXCL502 initially as a monotherapy and possibly as a combination with BXCL501 for the chronic treatment of agitation in patients with dementia or other stress-related illnesses. The active pharmaceutical ingredient ("API") underlying BXCL502 is designed to affect serotonergic signaling in the brain. Our preclinical data suggests BXCL502 has the potential to treat stress-related neuropsychiatric symptoms in dementia or other illness. In previously published third-party clinical trial data, daily administration of the API of BXCL502 demonstrated improvement in such behaviors using a well-established, clinically validated symptom scale. Formulation and clinical development planning are currently under way with BXCL502.

Neuroscience Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary products. The neuroscience and rare disease segments of the industry

are highly competitive. While we believe that our technology, development experience, and scientific knowledge provide competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical, and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions.

Many of our competitors may have significantly greater financial resources, and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining regulatory approvals, and marketing approved medicines than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and in establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, if any, the level of generic competition, and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize medicines that are safer, more effective, more convenient, less expensive, or have fewer or less severe side effects than any medicines we may develop. Our competitors also may obtain FDA or other regulatory approval for their medicines more rapidly than us, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic medicines. There are many generic medicines currently on the market for certain indications that we are pursuing, and additional generics are expected to become available over the coming years. We expect that any of our therapeutic product candidates that are approved will be priced at a significant premium over competitive generic medicines.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. IGALMI and any of our other product candidates that are approved, if any, will compete with the drugs discussed below, in addition to any other drugs currently in development.

Drugs used for the acute treatment of agitation related to schizophrenia and bipolar disorder are antipsychotics frequently administered via IM injection that typically requires patient restraint. These include IM aripiprazole, olanzapine, ziprasidone, and haloperidol. Oral products include the sublingually administered atypical antipsychotic asenapine, as well as benzodiazepines, lorazepam, and midazolam. The typical antipsychotic Adasuve (loxapine) from Alexza is delivered via inhalation.

Neuroscience Manufacturing

We do not have manufacturing facilities. We currently rely on strategic manufacturing partners, in particular ARx, LLC (“ARx”), and expect to continue to rely on third parties for the manufacture of our product candidates for clinical research and our products for commercialization efforts. ARx has agreed to exclusively manufacture and supply all of our worldwide supply of film formulation of dexmedetomidine to be used for the commercial supply of IGALMI and for ongoing clinical trials of BXCL501, subject to certain alternative supply provisions.

BXCL501 drug product is manufactured using commercially available components and packaging materials. The equipment employed for manufacture and analysis are consistent with standard pharmaceutical production.

Neuroscience Commercialization

We plan to retain worldwide commercialization rights for IGALMI and other approved product candidates, if any, but could consider collaboration opportunities to maximize returns or facilitate commercialization efforts in foreign jurisdictions. For additional information regarding our commercialization efforts for IGALMI, see above under “IGALMI Commercial Progress.”

We have limited experience commercializing products, however, in connection with the FDA approval of IGALMI, we have built out our in-house commercial organization and capabilities. We intend to leverage our in-house commercial organization, and will add to it where necessary, to support any additional approved product candidates. We may consider partnerships, joint ventures, and other business transactions and structures for markets outside the U.S.

As product candidates advance through our pipeline, our commercialization plans may change. Clinical data, the size of the development programs, the size of the target market, the required commercial infrastructure, and manufacturing needs may all influence global commercialization strategies.

Credit Facilities

In April 2022, we entered into financing agreements with affiliates of Oaktree Capital Management, L.P. and Qatar Investment Authority that provides for up to $260 million in gross funding to support the Company's commercial activities of IGALMI sublingual film and the expansion of clinical development efforts of BXCL501, which includes a Phase 3 program for the acute treatment of agitation in patients with Alzheimer's disease, and for general corporate purposes.

Neuroscience Intellectual Property

Our policy is to protect and enhance the proprietary technologies, inventions, and improvements that are commercially important to our business by filing patent applications in the U.S. and other jurisdictions related to our proprietary technology, inventions, improvements, and product candidates. We also rely on trademarks, trade secrets, and know-how relating to our proprietary technologies and product candidates, continuing innovation, and in-licensing technology and products. This reliance is expected to develop, maintain, and strengthen our proprietary position for novel therapeutics and novel formulations of existing therapeutics across multiple therapeutic areas. We also plan to rely on data exclusivity, market exclusivity, and patent term extensions when available.

We have multiple patent families filed to protect our neuroscience portfolio including the BXCL501 program. As of January 31, 2023, our neuroscience patent portfolio included four Patent Cooperation Treaty ("PCT") applications not yet in the national phase, 13 U.S. utility applications, five issued U.S. utility patents, four U.S. provisional patent applications, 87 pending non-U.S. applications, nine allowed or granted non-U.S. patents (including three in Japan), one design patent application, which is a U.S. design application, and 34 allowed or registered design patents (including two in Japan). Four U.S. patents (U.S. Pat. Nos. 10,792,246; 11,478,422; 11,497,711; and 11,517,524), directed to our proprietary sublingual film formulation of Dex and issued between 2020 and 2022 with an expiration date no earlier than 2039 are now listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). In the same family, we also have allowed/granted patents in mainland China, Taiwan, Australia, Mexico, Europe, and other countries in Asia, and pending applications in the U.S., China, and other major markets. We expect that patents issued in this family will expire no earlier than 2039. We have also filed applications in additional patent families that are relevant to BXCL501. We have applications pending in the U.S., Europe and Japan directed to methods of treating insomnia using sublingual Dex. We expect that patents issuing from these applications, if any, will expire no earlier than 2035. We also have applications filed in 16 regions, including the U.S., Europe, Japan, and China, directed to methods of treating agitation. We expect that patents issuing from these applications, if any, will expire no earlier than 2042. We have one U.S. application and one European application directed to intravenous administration of Dex. We expect that patents issuing from these applications, if any, will expire no earlier than 2039. We also have one PCT application directed to treating mania and another to treating depression. If patents issue from those cases, we expect them to expire no earlier than 2041 and 2042, respectively.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the U.S., the patent term is 20 years from the earliest filing date of a non-provisional patent application. Depending upon the timing, duration, and specifics of FDA approval of our product candidates, a U.S. patent that we own, or license, may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (a.k.a., the "Hatch-Waxman Act"). The act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the drug approval regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date

of an investigational new drug, and the submission date of a new drug application ("NDA"), plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension, and the application for extension must be made prior to patent expiration. The U.S. Patent and Trademark Office ("USPTO"), in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

The term of a patent can also be extended by Patent Term Adjustment ("PTA") established in 35 USC 154(b). The intention of the PTA is to accommodate for delays caused by the USPTO during the prosecution of a U.S. utility or plant patent application. Under PTA, the USPTO delay is divided into three types: type A (delays after 14 months from the filing date of the application until the USPTO issues a first Office Action and delays after four months from the filing of certain actions by the applicant until the USPTO responds to such actions); type B (delays after three years from the earliest effective filing date until a patent is granted); and type C (delays due to interferences, secrecy orders, and successful appeals). The total amount of PTA is calculated by adding the types A, B, and C delays, and then subtracting any delay that is overlapped among three types or that is attributable to the applicant.

The term of a patent can also be shortened by a terminal disclaimer. A terminal disclaimer is a statement filed by a patent owner in which the owner disclaims or dedicates to the public the terminal part of the term of a patent. Often, the terminal disclaimer is filed in cases where at least one claim of a pending application would have been obvious in light of at least one claim in an earlier-filed patent, AKA non-statutory obviousness-type double patenting rejection.

The patent positions of companies such as ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of method of use patents or reformulation patents has emerged in the U.S. Patent laws and their interpretation outside of the U.S. are also uncertain. Changes in either the patent laws or their interpretation in the U.S. and other countries may diminish our ability to protect our technology or product candidates and enforce the patent rights that we license and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions, and improvements. With respect to both licensed and company owned intellectual property, we cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use, or the manufacture of those products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and the issued patents that we in-license and those that may issue in the future may be challenged, invalidated, or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies outside the scope of the rights granted under any issued patents that we own or exclusively in license. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing, and regulatory review of a potential product, it is possible that, before any product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

Immuno-Oncology

On April 19, 2022, we announced the formation of a wholly owned subsidiary, OnkosXcel Therapeutics, LLC ("OnkosXcel") to develop potentially transformative medicines in oncology. OnkosXcel is our clinical-stage biopharmaceutical subsidiary using proprietary AI capabilities to drive the capital-efficient development of innovative anti-cancer therapeutics. Our approach to drug discovery leverages the application and methodology of EvolverAI, a proprietary AI-based research and development platform utilized in the successful development of IGALMI with the aim of efficiently identifying and developing immuno-oncology product candidates. We believe that BXCL701 reflects the

potential of this discovery approach in immuno-oncology. BXCL701 is an investigational, oral innate immune activator which demonstrated a 25% composite response rate in a Phase 2a clinical trial to treat patients with small cell neuroendocrine ("SCNC")-phenotype metastatic castration-resistant prostate cancer ("mCRPC"). We intend to initiate a Phase 2b trial in mCRPC patients with SCNC phenotype in the second half of 2023 following planned meetings with the FDA.

mCRPC is often characterized as a "cold" tumor, that is, a tumor with an immunosuppressive tumor microenvironment ("TME") and poor immune cell infiltration. Currently approved checkpoint inhibitors ("CPIs") that target programmed cell death 1 ("PD-1"), or cytotoxic T-lymphocyte-associated protein 4 have failed to demonstrate meaningful single-agent activity against such difficult-to-treat tumor types, including mCRPC. BXCL701 is designed to promote an immune induced inflammatory response in the TME primarily via inhibition of dipeptidyl peptidases ("DPP") 8 and 9, which we believe can provide for enhanced CPI therapeutic utility. We believe that BXCL701 can potentially provide significant benefits for the approximately 20% of the estimated 288,300 men who will be diagnosed with prostate cancer in the U.S. in 2023 and are expected to progress to the more aggressive mCRPC form of the disease, including approximately 20% (or approximately 11,532) of those patients who will develop the SCNC phenotype, for which there are currently limited treatment options.

Immune checkpoints represent a myriad of inhibitory pathways that act to regulate the duration and intensity of an antigen-induced immune response and factor prominently in mediating immune tolerance. They function as critical gatekeepers that prevent the indiscriminate attack of normal host cells by components of the immune system. Certain cancers co-opt these pathways and overexpress immune checkpoint molecules to camouflage themselves to avoid detection and destruction. CPIs, designed to harness the intrinsic power resident in the immune system, work by disabling the suppressive function of immune checkpoints, allowing the immune system to bypass such cancers' shield of immune tolerance. CPIs are expected to generate sales of more than $50 billion worldwide by 2025, up from sales of approximately $29 billion in 2020. While CPIs have proven to be a significant advancement in cancer therapy, those currently approved by the FDA do not produce meaningful results in a majority of patients, as the clinical benefit is generally viewed to be limited to between 13% and 30% of cancer patients, and the duration of response is relatively short.

We believe the limited efficacy of approved CPIs results primarily from their intervention at later stages of the immune response. As a result, other targets and pathways can be exploited by the tumor to create a TME that can evade the enhanced immunological response enabled by approved CPIs. While numerous agents designed to target the earlier stages of an immune response are in development for use in combination with CPIs, their activity is restricted to a single component of the immune response. In contrast, we have developed BXCL701 to simultaneously address multiple components of the immune response, including:

- *Cancer antigen presentation by dendritic cells*: stimulation of dendritic cell trafficking to tumor draining lymph nodes.
- *Priming and activation of T cells*: acceleration of tumor-induced priming of T cells and the formation of potent cytotoxic T lymphocytes ("CTLs").
- *Infiltration of immune cells into the tumor*: stimulation of release of chemokines that attract effector T cells but block regulatory T cells, and also induce NK cell and neutrophil migration.
- *Killing of tumor cells*: induction of formation of CTLs and NK cells expressing tumor-killing perforins and granzymes, as well as the formation of memory T cells that can selectively kill returning tumor cells.

Accordingly, we believe BXCL701 may have utility in stimulating increased activation, proliferation, and infiltration of tumor cells by immune effector cells, enabling its potential application in combination with currently approved CPIs, across a range of hematological malignancies and solid tumors, to potentially:

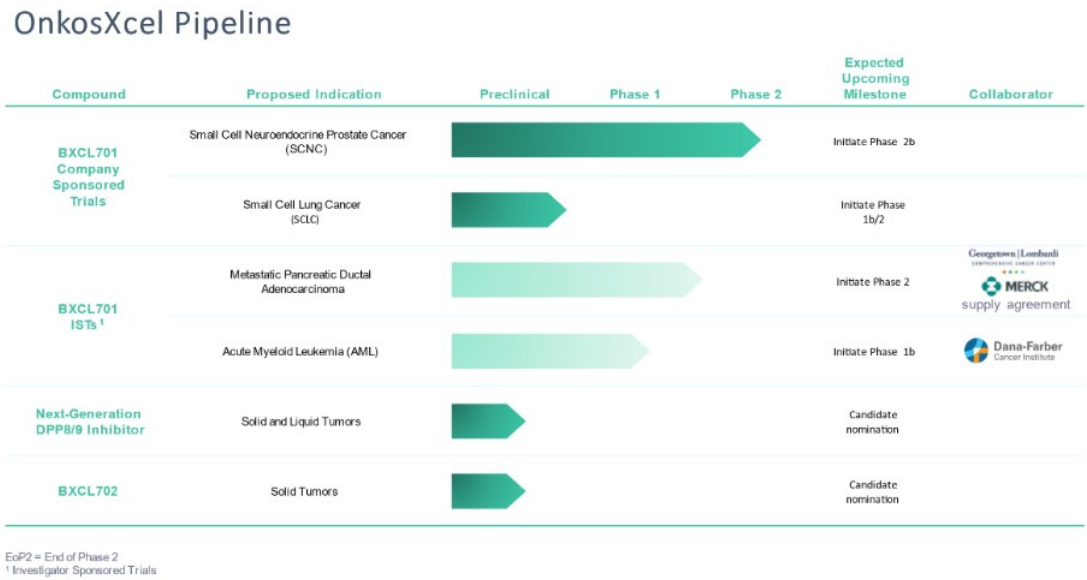
- *Convert immunological cold tumors into ones sensitive to CPIs;*
- *Enhance hot tumors' response rate and depth of response to CPIs; and*

- *Restore CPI sensitivity to tumors that were previously responsive.*

Central to our drug discovery initiatives are proprietary, AI-driven platform technologies we employ to identify novel therapeutic uses for approved therapeutics and candidates in clinical evaluation. The first and more advanced of our AI-driven discovery programs is our innate immune modulation program, which supported the pursuit of BXCL701 as a development candidate. We believe the application of this program provides us actionable insights into the inflammasome, a component of the innate immune system responsible for activation of the inflammatory response. We also believe that novel therapeutic approaches to indications of unmet medical need may also emerge from the intersection of innate immunity modulation and synthetic lethality, an approach focused on the identification of cancer-promoting gene pairs with driver mutations whose concomitant disruption activates PD-1. We are working to develop our second AI-driven product candidate, BXCL702, by leveraging our innate immunity modulation program and/or our synthetic lethality program, via re-innovation or in-licensing and we intend to nominate a candidate by 2025.

Our Immuno-Oncology Programs

Below is a summary of the status of our immuno-oncology clinical development programs as of the date of this Annual Report on Form 10-K. We believe our product candidates, if successfully developed and approved, have the potential to become compelling treatment options for their respective indications.



An Overview of the Immune System

The immune system is a host defense system comprised of multiple structures and processes within an organism that protects against disease. As with other mammalian species, the human immune system is comprised of the innate immune system and the adaptive immune system. The innate immune system involves an immediate, non-specific response to infected or diseased cells. Triggering its activation are pathogen-associated and damage-associated molecular patterns recognized by pattern recognition receptors (“PRRs”), which reside on the surface of various types of leukocytes, or white blood cells, which make up the innate immune system including phagocytes, eosinophils, and natural killer cells. The innate immune response also participates in promoting activity of the adaptive immune system.

The adaptive immune system is made up of special types of leukocytes known as T and B lymphocytes, or T cells and B cells, respectively. T cells participate primarily in the cell-mediated immune response while B cells are involved in the humoral immune response. T lymphocytes can be further segregated into distinct cell types, with the primary types

being CD8, or cytotoxic, T cells and CD4 T cells. CTLs directly eliminate cells that are infected with viruses or other pathogens or are otherwise damaged or dysfunctional. Anti-cancer activity is primarily CD8 T cell mediated. CD4 T cells, which have limited cytotoxic activity, mediate the activity of other cells to eliminate pathogens. Activation of a resting CD4 T cell causes it to release cytokines that influence the activity of an array of cell types. Cytokines released by activated Type 1 CD4 T cells enhance the microbicidal activity of macrophages and the activity of CD8 T cells.

A critical capability of the immune system is its ability to distinguish between healthy, functioning host cells and either non-self-infectious agents or damaged or dysfunctional host cells. The ability to differentiate between these entities is the central feature of immune tolerance. A significant limitation of currently approved therapeutics against endogenous diseases such as cancer is the inability to overcome host immune tolerance and elicit a strong, target-specific immune response while avoiding off-target complications.

Immune Tolerance and the Role of Immune Checkpoints

The immune system's ability to distinguish between a normal, healthy cell and an infected, damaged, dysfunctional, or cancer cell is accomplished through an immunological selection process that occurs in the thymus during early development. Antigen specific immune cells, such as T cells, B cells and NK cells, which recognize molecular markers originating from normal, healthy tissues are eliminated in the thymic medulla to avoid possible autoimmune consequences through a negative selection process. This results in the suppression of immune effector cell activation and proliferation. Immune checkpoints represent a myriad of inhibitory pathways that act to regulate the duration and intensity of antigen-induced immune responses and factor prominently in mediating immune tolerance. A number of checkpoint molecules have been identified and studied in cancer therapy in the past decades. Two of the more well-characterized immune checkpoint molecules are CTLA-4 and PD-1, and its related ligand, PD-L1.

As key regulators of the immune system, immune checkpoints are critical gatekeepers that prevent the indiscriminate attack of normal host cells by components of the immune system. Their suppressive function usually depends on ligand-induced signaling, with protein structures on the surface of immune effector cells binding to complementary molecular structures on partnered cells. This signaling not only dampens the generation of co-stimulatory cytokines instrumental in triggering and sustaining a robust immune response, such as interleukin 2 and interferon gamma, but also results in an upregulation of regulatory T cells, which acts to further suppress immune effector cell activity. These factors bias the immune response towards anergy and senescence rather than activation and proliferation. Certain tumors coopt these pathways and overexpress immune checkpoint molecules on their cell surface to camouflage themselves to evade detection and destruction by the immune system.

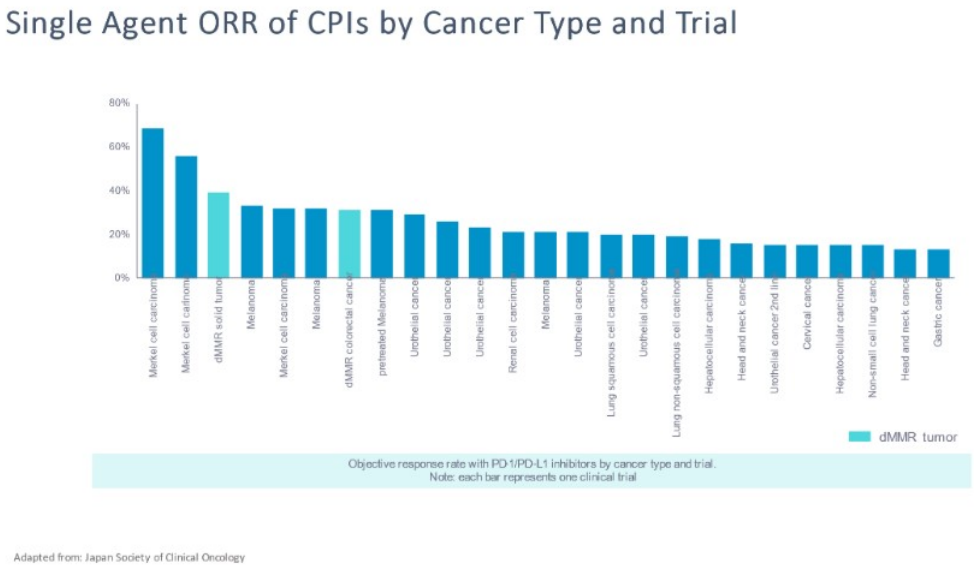
Immunotherapy and the Emergence of Checkpoint Inhibitors

Cancer immunotherapy, designed to harness the intrinsic power resident in the immune system by modulating immune cell function, has proven to be a major advancement in cancer treatment. Immune CPIs have emerged as one of the most promising classes of cancer immunotherapy. CPIs work by disabling the inhibitory function of immune checkpoint proteins. Disabling immune checkpoints allows the immune system to bypass the shield of immune tolerance the checkpoints provide, allowing the tumor-directed immune effector cells to engage the tumor. Seven CPIs targeting PD1/PD-L1 and CTLA-4 have been approved by the FDA to treat more than a dozen different types of cancer. CPIs directed towards other validated checkpoints, including lymphocyte activation gene 3 and T cell immunoreceptor with immunoglobulin and ITIM domain have recently been approved or are advancing through clinical development. These CPIs are largely involved in modulating the activity of the adaptive immune system. Immune checkpoint molecules, such as CD47, which regulate responses mediated by the innate immune system, are also under evaluation as potential therapeutic targets for checkpoint inhibition. CPIs across a spectrum of cancer types are expected to generate sales of more than $50 billion worldwide by 2025, up from sales of $29 billion in 2020.

Limitations of current approaches

While CPIs have proven to be a significant advancement in cancer therapy, those currently approved by the FDA do not produce meaningful results in a majority of patients: clinical benefit is generally viewed to be limited to between 13% and 30% of cancer patients and the duration of response to treatment is often short. CPIs require the infiltration of anti-tumor CD8 T cells for therapeutic activity, and patients whose tumors are characterized by a TME that lacks

activated TILs, typically fail to respond to therapy. Moreover, the expression of positive costimulatory signals is critical to the amplification and diversification of a TIL-based response following initial activation, without which treatment durability is limited. We are focused on advancing therapeutic candidates designed to overcome these challenges and enhance the sensitivity of immunologically inaccessible, or cold, tumors to an efficacious immune response. The chart below shows the single agent objective response rate ("ORR") of CPIs by different cancer types and clinical trial.



Adapted from: Japan Society of Clinical Oncology

Immuno-Oncology Clinical Trials

Leveraging the insights enabled by the application and methodology of EvolverAI, a proprietary AI-based platform used to identify novel therapeutic uses for approved therapeutics and product candidates in clinical evaluation, and our internal industry expertise, we are pursuing two proprietary discovery programs to advance our goal of developing anti-cancer therapeutics. The first program, which encompasses BXCL701 across a range of indications, is based on the application of innate immune modulation technology. This program has been constructed to embrace key distinguishing characteristics of the innate immune system and we believe it is supported by our development efforts. This approach has driven the development of BXCL701, which we are currently evaluating in a Phase 2 clinical trial as a potential treatment for mCRPC with SCNC phenotype. Fundamental to the innate immune modulation program is BXCL701's potential to:

- Convert cold tumors into ones sensitive to CPIs;
- Enhance hot tumors' response rate and depth of response to CPIs; and
- Restore CPI sensitivity to tumors which had previously been responsive.

Encouraged by the positive results of BXCL701 in our Phase 2a trial, we are working towards nomination of a next-generation DPP8/9 inhibitor for the same indications and to target additional difficult-to-treat solid and liquid tumors.

We believe that novel therapeutic approaches to indications of unmet medical need may also emerge from the intersection of innate immunity modulation and synthetic lethality, an approach focused on the identification of cancer-promoting gene pairs with driver mutations whose concomitant disruption activates PD-1. We are working to develop our second AI-driven product candidate, BXCL702, leveraging our innate immunity modulation program and/or our

synthetic lethality program, via re-innovation or in-licensing. We anticipate nominating a clinical candidate in this program by 2025, at which time we intend to submit an investigational new drug application ("IND") to the FDA.

BXCL701 Innate Immune Activator

BXCL701 (talabostat) is an oral small molecule inhibitor of a class of enzymes called DPPs, specifically DPP8/9 and DPP4. Inhibition of DPP8/9 initiates activation of the inflammasome and ultimately activation of the innate immune system. Key characteristics of BXCL701 include:

- Orally bioavailable, potentially sole inhibitor of both DPP8/9 and DPP4, key regulators of the inflammasome directed innate immune response, currently in clinical development for cancer.
- Novel proposed mechanism of action may complement CPI activity, enabling therapeutic access to immunologically cold tumors as well as other difficult-to-treat cancers, including relapsed or refractory tumor types.
- Phase 2 clinical proof-of-concept achieved in treating mCRPC patients with either adenocarcinoma or SCNC phenotype.

Initial focus on mCRPC with SCNC phenotype designed to provide for a more efficient clinical development pathway than current industry standards.

BXCL701 as a potential treatment for mCRPC

Prostate cancer is the most common malignancy and the second-leading cause of cancer-related deaths in men in the U.S. According to the American Cancer Society, approximately 288,300 men will be diagnosed with, and more than 34,700 men will die of, prostate cancer in 2023. The majority of these cases will be classified as adenocarcinomas and involve low risk, localized or regional disease for which the five-year survival rate ranges from 60% to 99%. However, an estimated 20% of these newly diagnosed cases will progress to the more aggressive metastatic disease. The five-year survival rate for men with metastatic prostate cancer drops significantly, to approximately 30%. Approximately 20% of patients with mCRPC will develop SCNC phenotype, which is characterized by poor prognosis and low survival rate with a five-year life expectancy of 14%.

Prostate function requires the presence of various androgens, such as testosterone. Early cancerous prostate cells typically also require androgens to proliferate. Accordingly, aggressive forms of prostate cancer can initially be treated using androgen deprivation therapy ("ADT"). While ADT offers temporary therapeutic benefit, in almost all patients the treatment eventually loses efficacy, referred to as "castration resistance." Cases of castration-resistant prostate cancer ("CRPC") are generally treated with a second-generation androgen receptor ("AR") inhibitor, such as XTANDI (enzalutamide), or an androgen synthesis inhibitor, such as ZYTIGA (abiraterone), which targets the enzyme CYP17 to block the production of testosterone. These therapeutics have widely become the standard of care, though only ZYTIGA has been approved to treat mCRPC, as well as metastatic high-risk castration-sensitive prostate cancer. XTANDI has been approved to treat CRPC and metastatic castration-sensitive prostate cancer.

Virtually all patients who respond to ZYTIGA and XTANDI are expected to progress to even more aggressive forms of prostate cancer requiring further treatment. Patients whose disease has progressed after treatment with these second-generation targeted endocrine therapies are administered a docetaxel containing drug regimen that provides a survival benefit of only 10 months. The poly-ADP ribose polymerase ("PARP") inhibitors LYNPARZA (olaparib) and RUBRACA (rucaparib) are approved for the treatment of mCRPC in patients whose disease has progressed after receiving XTANDI or ZYTIGA, but their approval is limited to instances of mCRPC linked to a BRCA gene mutation. As such, an unmet medical need remains for patients with mCRPC who are not eligible for PARP inhibitor treatment after treatment with the targeted endocrine therapy and docetaxel.

In addition, a number of men, both newly diagnosed patients and men whose disease has progressed after second-generation targeted endocrine therapy, will develop an aggressive tumor that expresses very little AR and accordingly does not respond to therapeutics targeting the AR signaling pathway. Prostate cancer with this phenotype is referred to as SCNC, for which there is currently no effective treatment. The incidence of SCNC is increasing with the widespread use

of AR inhibitor therapy. Treatment protocols for patients with SCNC typically involve cytotoxic chemotherapies despite their short duration of response and considerable toxicities. These patients represent an additional unmet medical need among men with prostate cancer. We believe BXCL701 may prove efficacious in addressing the unmet needs of both adenocarcinoma and SCNC prostate cancer phenotypes.

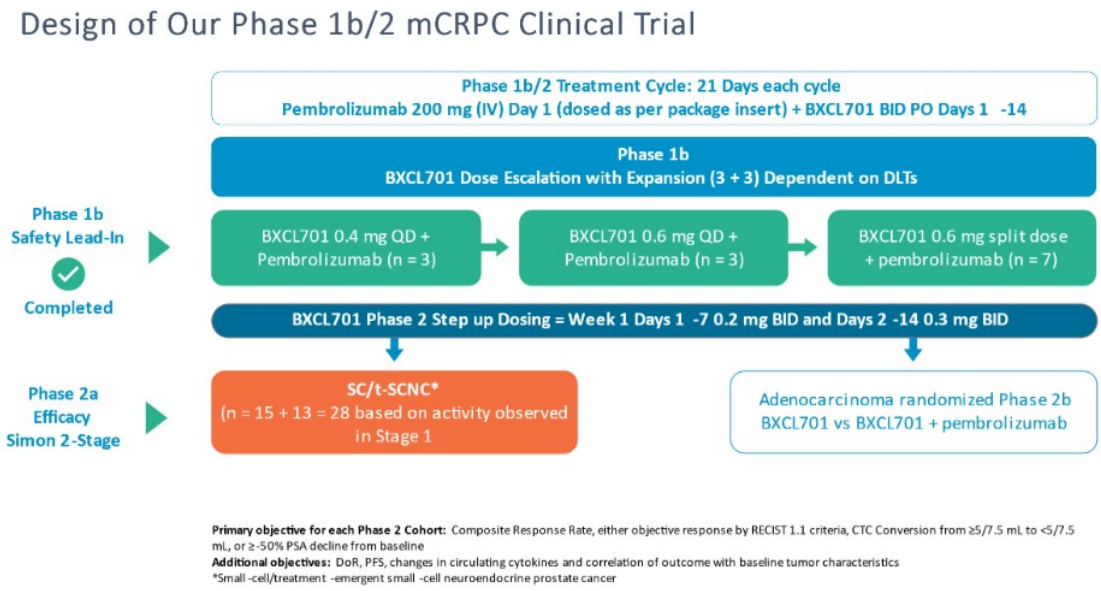
mCRPC is often characterized as a cold tumor, or a tumor with an immunosuppressive TME and poor immune cell infiltration. Currently approved CPIs, which target PD-1 and CTLA-4, have not demonstrated significant single-agent therapeutic utility. For instance, a Phase 2 investigator sponsored trial ("IST") to assess the efficacy of the PD-L1 inhibitor avelumab, marketed by EMD Serono and Pfizer as BAVENCIO, to treat mCRPC with SCNC phenotype, as well as aggressive variant prostate cancer with adenocarcinoma histology, generated an ORR of 6.7% (representing 1 of 15 patients who was known to be microsatellite instability-high, an established marker of response to CPIs).

We believe the limited efficacy of CPIs results primarily from their intervention at later stages of the immune response. As a result, other targets and pathways can be exploited by the tumor to create a TME that can evade the enhanced immunological response enabled by approved CPIs. BXCL701 is designed to act on multiple components of immune system functioning, including:

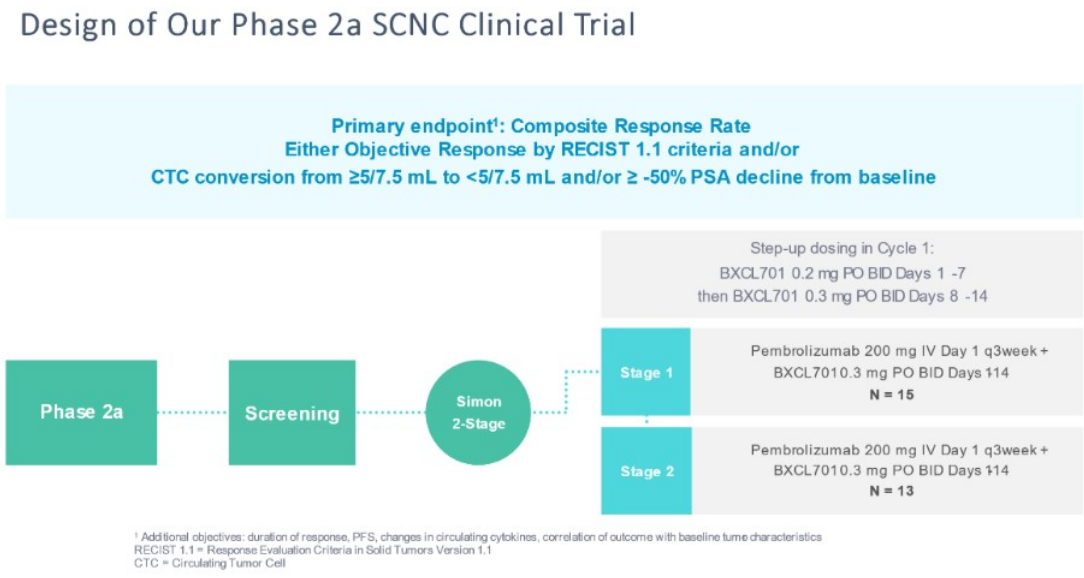
- *Cancer antigen presentation by dendritic cells*: stimulation of dendritic cell trafficking to tumor draining lymph nodes.
- *Priming and activation of T cells*: acceleration of tumor-induced priming of T cells and the formation of potent CTLs.
- *Infiltration of immune cells into the tumor*: stimulation of release of chemokines that attract effector T cells but block regulatory T cells and also induce NK cell and neutrophil migration.
- *Killing of tumor cells*: induction of formation of CTLs and NK cells expressing tumor-killing perforins and granzymes as well as the formation of memory T cells that can selectively kill returning tumor cells.

We believe BXCL701 may have utility in stimulating increased activation, proliferation and infiltration of tumor cells by immune effector cells enabling its potential use in combination with currently approved CPIs to treat cold tumors, such as mCRPC. We elected to pursue mCRPC as an indication for BXCL701 due to its enrichment for DPP mutations, which are especially prevalent in tumors with SCNC phenotype.

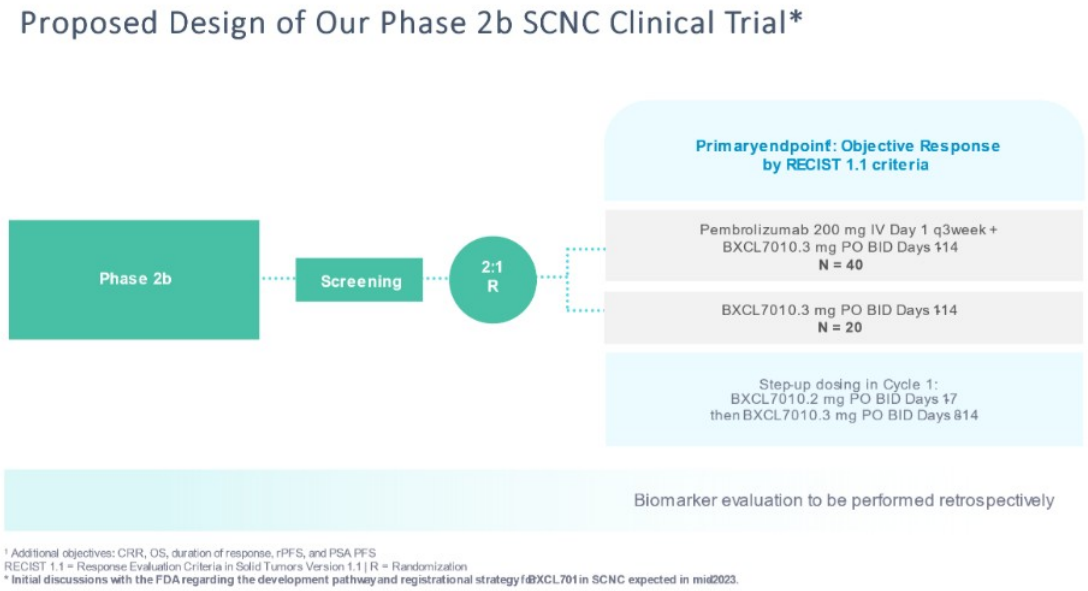
BXCL701 is being evaluated in the Phase1b/2 clinical proof-of-concept trial that we are sponsoring, to investigate its efficacy when used in combination with pembrolizumab. We intend to initiate the Phase 2b portion of the trial in the second half of 2023. We are also planning to meet with the FDA in the second half of 2023 to discuss the ability of our Phase 2b trial to serve as a potential registrational trial.



The Phase 1b portion of our Phase 1b/2 clinical trial was a dose escalation safety lead-in which employed a standard 3 x 3 trial design to determine the recommended Phase 2 dose. During each 21-day treatment cycle, 200mg of pembrolizumab were administered intravenously on day one, with BXCL701 taken twice daily on days one through 14, for a minimum of two cycles. The results of this Phase 1b trial, which were presented at The Society for Immunotherapy of Cancer's 35th Anniversary Annual Meeting, allowed us to establish 0.3mg, taken twice daily, as the recommended Phase 2 dose.



The Phase 2a portion of the trial was segregated into two 28-patient trial cohorts, one cohort consisting of mCRPC patients with SCNC phenotype and a second cohort consisting of mCRPC patients with adenocarcinoma phenotype. Initially, we focused on mCRPC with SCNC phenotype as the primary indication for BXCL701, since DPP9 is amplified in approximately 17% of treatment-emergent mCRPC with SCNC phenotype, compared to 5% or less in the broader prostate cancer population. However, we also observed responses in mCRPC patients with adenocarcinoma phenotype who were microsatellite stable in our Phase 1b trial. On this basis, we widened our Phase 2a trial to include relapsed mCRPC patients with either SCNC or adenocarcinoma phenotype. Both cohorts employed a Simon two-stage trial design of 15 trial participants followed by 13 additional patients. The primary endpoint of the Phase 2a portion of this trial was a composite response rate, determined as either a RECIST 1.1 response (defined as a reduction in RECIST score of 30% or more), a reduction in prostate specific antigen ("PSA") level of 50% or more, or conversion in circulating tumor cells ("CTCs") from 5 or more CTCs/7.5 milliliter ("ml") to less than 5 CTCs/7.5ml. Secondary endpoints included duration of response, progression free survival, changes in circulating cytokines and certain disease-specific biomarkers. Based on these results, we intend to pursue expansion of the Phase 2a trial involving mCRPC patients with SCNC phenotype into a Phase 2b trial, which we expect would enroll 60 patients subject to further changes as we seek regulatory guidance. We intend to meet with the FDA in the second half of 2023 to discuss our plan to design the Phase 2b trial to serve as a potential registrational trial.



We believe the final results observed in the Phase 2a trial of BXCL701 administered in combination with pembrolizumab support further development. Our Phase 2a study is not a controlled study comparing the safety and efficacy of pembrolizumab alone against BXCL701 and pembrolizumab for the treatment of SCNC.

We were particularly encouraged by the results observed in the cohort consisting of mCRPC patients with SCNC phenotype. Final Phase 2a results for the SCNC cohort were presented at the 2023 Genitourinary Cancers Symposium of the American Society of Clinical Oncology ("ASCO GU 2023"). BXCL701 in combination with pembrolizumab demonstrated a 25% (seven out of 28 evaluable patients) composite response rate in mCRPC patients with SCNC phenotype, for whom there is no standard of care. As of December 19, 2022, the median duration of response for the seven composite responders was 6+ months (range 1.3 – 17.4 months). Five of these responders were RECIST 1.1 responders (four confirmed responses and one unconfirmed) with decreases in tumor size ranging from 42% to 67% and a median duration of response of 6+ months (range 1.3 – 17.4 months). The sixth responder was a CTC and PSA50 responder, with a PSA decrease of 73%. The seventh responder was a PSA50 responder, with a PSA decrease of 50%.

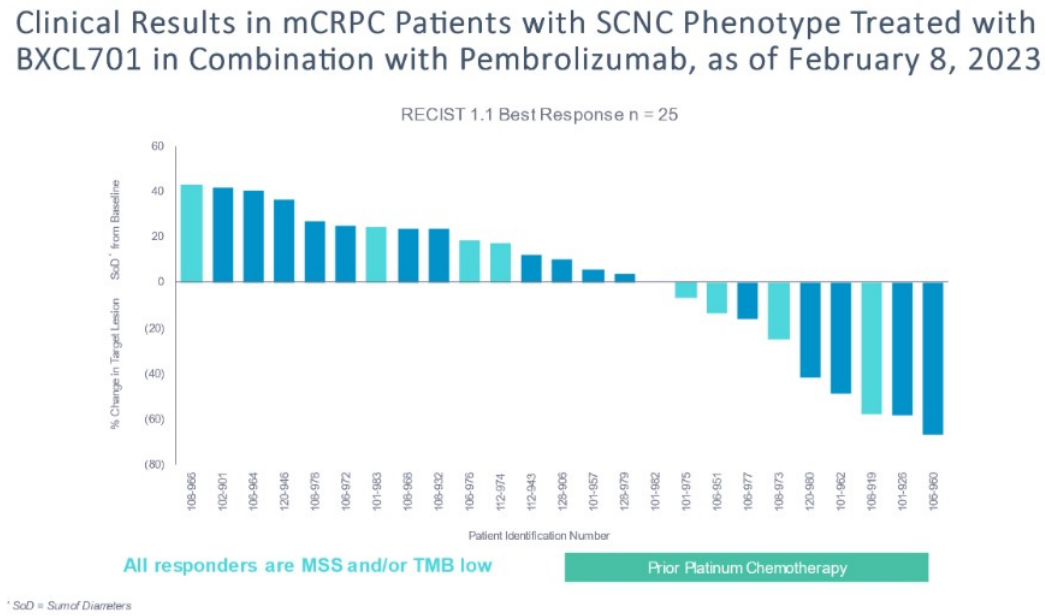
Final Clinical Results From the 7 Composite Responders in the Phase 2a SCNC Cohort, as of December 19, 2022

Patient	Prior Systemic Therapies	Duration on Treatment (weeks)	RECIST 1.1 ≥-30%[2]	CTC ≥5/7.5 ml to <5/7.5 ml[2]	PSA ≥-50%[2]	Tumor Biology
106-960	Bicalutamide, Lupron carboplatin, etoposide	65.7	-67% Confirmed		NA	TMB = 3 MSS
108-919[1]	Degarelix, Lupron	19 (+ 18 off treatment)	-58% Confirmed		NA	TMB = 0 MSS
101-926[1]	Abiraterone, leuprolide, chemoradiation, abiraterone, prednisone, cisplatin, etoposide	18	-58% Unconfirmed	1 to 0	NA	MSS
101-962	ADT, carboplatin / docetaxel	47	-49% Confirmed		NA	TMB = 4
120-980	Carboplatin, Etoposide, Prostap	24	-42% Confirmed	NA	NA	TMB = 2.9
108-953[1]	Degarelix, Lupron, arboplatin/docetaxel	70	SD 64 weeks	19 to 4	-73%	MSS PD-L1 low
112-974[1]	Abiraterone, bicalutamide, docetaxel	7.6	+17%	117 to 47	-50%	TMB = 4 MSS

On Treatment Off Treatment Response

[1] Tissue used in exploratory biomarker analysis
[2] Change from baseline | TMB = Tumor Mutation Burden | MSS = Microsatellite Stable

The Phase 2a results for the SCNC cohort presented at ASCO GU 2023 demonstrated that, as of December 19, 2022, among the 28 evaluable patients, 25 of whom had RECIST measurable disease, the composite response rate was 25% (with RECIST response rate of 20%, disease control rate of 48% and CTC conversion rate of 25%). Of note, based on published data from mCRPC patients with SCNC phenotype, a response to pembrolizumab monotherapy has generally been limited to those patients whose tumors are remarkable for their high levels of genetic mutations associated with microsatellite instability, yet only one responder in the adenocarcinoma cohort, had this molecular predictor of pembrolizumab response, and all seven responders in the SCNC cohort were microsatellite stable and/or tumor mutational burden low. We believe the response rates in the absence of a high tumor mutational burden observed in our Phase 2a trial results reinforce the synergistic interaction between BXCL701 and pembrolizumab. Presented below are the results (as of February 8, 2023) for the 25 evaluable mCRPC patients with SCNC phenotype with RECIST measurable disease. These results were presented at ASCO GU 2023.

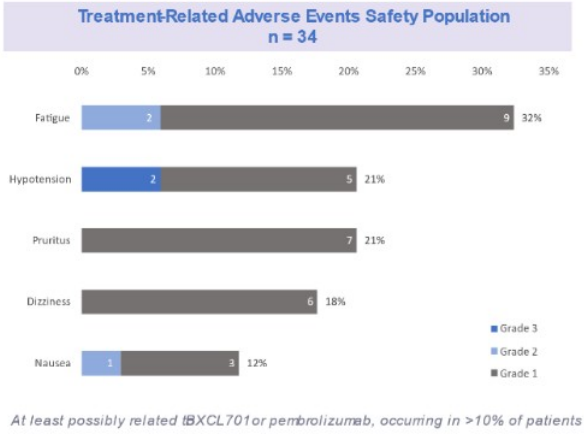


AEs consistent with cytokine activation, including fever, nausea, chills, fatigue, headache, and dizziness were observed during the trial and were generally mild to moderate. SAEs experienced by six trial participants - one patient hospitalized with Grade 1 orthostatic hypotension, one patient hospitalized with Grade 3 hypotension and acute kidney injury (“AKI”), which resolved, one patient with Grade 3 hypothyroidism which resolved, one patient with Grade 3 colitis, one patient with Grade 3 generalized oedema, and one patient hospitalized with Grade 4/5 tumor lysis syndrome/AKI, which resulted in fatality after the patient voluntarily discontinued dialysis - were reported as related or possibly related to BXCL701 or pembrolizumab, though there was no evidence that BXCL701 potentiated immune-related AEs associated with CPIs. The table below summarizes treatment-related AEs observed in the SCNC cohort as of December 19, 2022.

AEs Observed in mCRPC Patients With SCNC Phenotype Treated With BXCL701 in Combination With Pembrolizumab, as of December 19, 2022

Treatment-Emergent Adverse Events n = 34	n (%)
Any Grade	33 (97%)
Attributed to BXCL701	29 (85%)
Attributed to Pembrolizumab	23 (68%)
Grade 3	16 (47%)
Grade 4	0
Grade 5	1* (3%)
AE Leading to Treatment Discontinuation	6 (18%)
BXCL701 Discontinuation	6 (18%)
Pembrolizumab Discontinuation	5 (15%)
Immune Related Adverse Events Any Grade	14 (41%)
Grade ≥3	1** (7%)

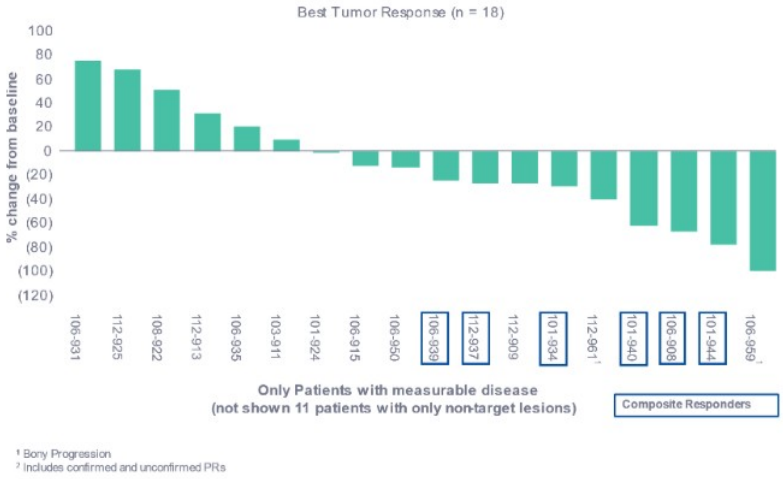
* Grade 5 tumor lysis syndrome
** Grade 3 Colitis



At least possibly related tBXCL701or pembrolizumab, occurring in >10% of patients

The Phase 2a trial has also been completed for the adenocarcinoma cohort. Preliminary results for this trial cohort were presented at the 2022 ASCO Genitourinary Cancers Symposium. In contrast to the typical low single digit response rate with the use of pembrolizumab as a standalone therapy in mCRPC patients seen in publications to date, we noted that among the 29 patients in the adenocarcinoma treatment arm who were evaluable for a composite response, all of whom received BXCL701 plus pembrolizumab, the composite response rate achieved was 21%. This included 22% who achieved a RECIST-defined partial response and a disease control rate, which reflects those patients with either a complete response, a partial response or stable disease, of 83%. Patients who stayed on therapy for at least two cycles of treatment and underwent at least the initial disease assessment at nine weeks were considered response evaluable for this trial, as specified in the trial protocol. Presented below are the preliminary results of this combination therapy in patients with measurable disease. Those patients with bone disease only, common among patients with metastatic prostate cancer, were excluded from this analysis, as bone lesions are considered non-target lesions in RECIST 1.1.

Preliminary Clinical Results in mCRPC Patients with Adenocarcinoma Phenotype Treated with BXCL701 in Combination with Pembrolizumab, as of November 24, 2021



[1] Bony Progression
[2] Includes confirmed and unconfirmed PRs

The majority of AEs experienced by patients in the adenocarcinoma cohort were low grade. AEs consistent with cytokine activation were observed, including fever, myalgia, nausea, chills, fatigue, dyspnea, headache and dizziness. SAEs experienced by five patients (12%) were reported as possibly related to BXCL701 or pembrolizumab: two reports of hypotension; one report of dizziness; one report of peripheral edema; one report of pyrexia; one report of Myasthenia Gravis; and one report of Cytokine Release Syndrome. Two patients (5%) discontinued therapy due to AEs. There was no evidence that BXCL701 potentiated immune-related AEs related to CPIs. The table below summarizes treatment-related AEs observed in the adenocarcinoma cohort.

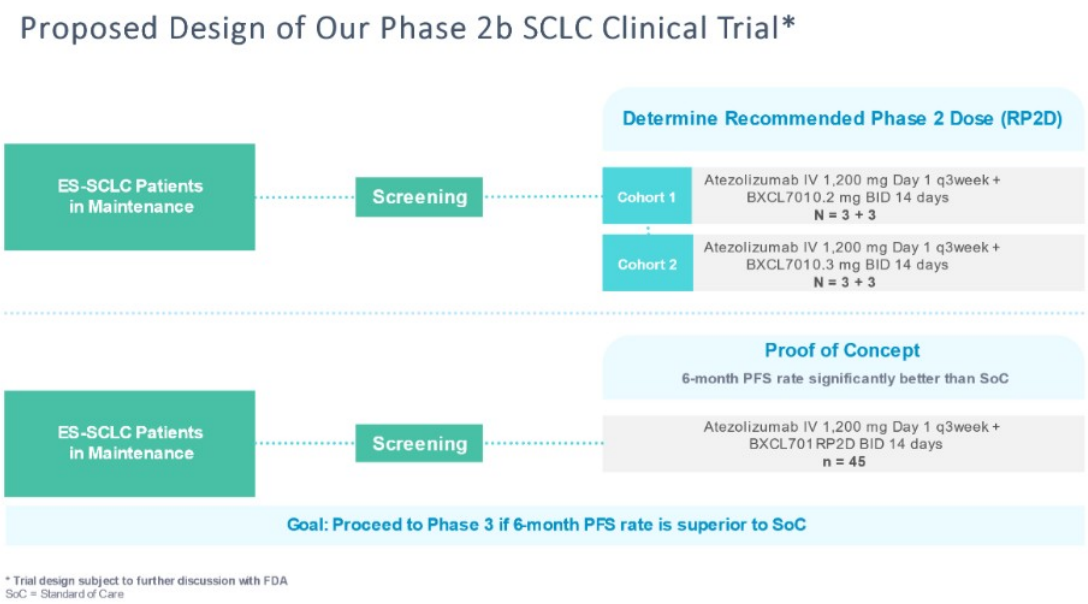
AEs Observed in mCRPC Patients with Adenocarcinoma Phenotype Treated with BXCL701 in Combination with Pembrolizumab, as of November 24, 2021

Treatment Related Adverse Events*	N = 42 N (%) Patients Reporting AE	
AE Preferred Term	Any Grade	Grade ≥ 3
Fatigue	18 (43)	
Nausea	13 (31)	
Vomiting	9 (21)	
Dizziness	8 (19)	1 (2)
White Blood Cell Count Decreased	8 (19)	1 (2)
Decreased Appetite	7 (17)	
Hypotension	7 (17)	2 (5)
Platelet Count Decreased	7 (17)	
Pruritus	7 (17)	
Anemia	5 (12)	2 (5)
Diarrhea	5 (12)	
Dry Mouth	5 (12)	
Hypoalbuminaemia	5 (12)	1 (2)
Hypothyroidism	5 (12)	

BXCL701 as a potential treatment for small cell lung cancer (“SCLC”)

The American Cancer Society estimates that in 2023, about 35,751 cases of SCLC will be diagnosed in the U.S. Approximately 60-70% of these patients present with extensive disease, and first-line therapy for a majority of these patients involves the combination of a CPI with platinum-based chemotherapy or etoposide.

We are encouraged by the therapeutic potential of BXCL701 for SCLC given the activity it has demonstrated in the ongoing SCNC clinical trial, and we plan to initiate clinical trials targeting this indication. We are planning to conduct a Phase 1b/2 trial designed to be a dose escalation safety lead-in to establish a recommended Phase 2 dose (“RP2D”). The Phase 2 portion of the trial is anticipated to involve 45 patients administered the RP2D of BXCL701 plus atezolizumab for nine treatment cycles over a six-month period. Should the combination of BXCL701 and atezolizumab achieve a rate of progression-free survival superior to that achieved using the standard of care in the Phase 2 proof-of-concept portion of the trial, we intend to advance BXCL701 into a Phase 3 clinical trial in SCLC.



We currently expect to initiate the Phase 1b portion of the trial in the second half of 2023 and the Phase 2 proof-of-concept portion of the trial in 2024.

BXCL701 as a potential treatment for other cancers

In addition to its potential use in combination with CPIs to treat mCRPC, an immunologically cold tumor, we are developing BXCL701 as a therapeutic for pancreatic cancer, and other solid tumors with greater, or "non-cold," immunological activity that are nonetheless regarded as difficult-to-treat, and hematological malignancies. We believe the synergistic potential of BXCL701 and CPIs, when administered in combination, could increase cancer cell susceptibility to an enhanced immune response, potentially increasing the clinical benefit of CPIs, whose single-agent efficacy in treating these tumor types is generally viewed to be limited to between 13% and 30% of cancer patients and the duration of response to treatment is often short. As such, we envision the potential therapeutic benefit of BXCL701 increasing the sensitivity of cold tumors to CPI therapy, enabling the potential treatment of a range of cancers including pancreatic cancer, breast cancer, colorectal cancer, and ovarian cancer, as well as enhancing the depth of response to CPIs in other cancers. In addition, based on the preclinical observation that BXCL701 showed direct cytotoxic activity against certain leukemic cells, we have initiated clinical development targeting relapsed or refractory acute myeloid leukemia ("AML").

Pancreatic Cancer

The American Cancer Society estimates that in 2023, about 64,050 cases of pancreatic cancer will be diagnosed in the U.S. We are supporting a Phase 2 IST sponsored by the Georgetown Lombardi Comprehensive Cancer Center ("Georgetown Lombardi"), designed to evaluate the use of BXCL701 along with pembrolizumab to treat pancreatic cancer. Few therapeutic options are available for patients with this indication, which has a five-year survival rate of less than 10%, among the lowest of all cancers. Pancreatic cancer has among the highest levels of overexpression and amplification of DPPs. Preclinical models demonstrated synergy between DPP inhibition with BXCL701 and anti-PD-1 antibody in the pancreatic cancer tumor microenvironment. Based on these preclinical observations, Georgetown Lombardi intends to assess the safety of BXCL701 when administered in combination with pembrolizumab, as well as estimate the 18-week progression-free survival rate. This trial is expected to begin in the second quarter of 2023.

Relapsed or refractory AML

The American Cancer Society estimates that in 2023, about 20,380 new cases of AML will be diagnosed in the U.S. We are supporting a Phase 1b IST sponsored by the Dana-Farber Cancer Institute ("Dana-Farber") designed to evaluate the use of BXCL701, along with the current standard of care to treat relapsed or refractory AML. We believe that pyroptosis triggered by BXCL701 may provide potent single agent cytotoxicity directed towards AML. We also believe that DPP9 copy number may provide an actionable biomarker, as high copy number has been observed to correlate with BXCL701 toxicity in human AML cell lines. DPP8/9 inhibition has been shown to be cytotoxic to THP-1 cells, monocytic cancer cells cultured from a patient with AML, but not other cell lines, suggesting a specific vulnerability of AML to these inhibitors which we believe can be exploited for therapeutic benefit. Based on these preclinical observations, Dana-Farber has initiated a Phase 1b trial to determine the maximum tolerated dose or the recommended Phase 2 dose of BXCL701 as a single agent, and to assess the safety of BXCL701. This trial began in the first quarter of 2023. Subject to successful completion of this Phase 1b trial, it is anticipated that Dana-Farber will conduct further studies to determine BXCL701's objective response rate in AML in combination with the standard of care.

Other potential anti-cancer programs

We collaborated with the University of Texas MD Anderson Cancer Center in a Phase 2a IST to evaluate the potential efficacy of BXCL701 administered in combination with pembrolizumab in patients with advanced solid cancer. The design of this open label trial includes two cohorts and incorporates a two-stage configuration, which allows for an expansion of patient enrollment to a total of 17 patients in each cohort if a RECIST 1.1 complete response or partial response is observed in at least one of the initial nine patients. The first cohort enrolled patients who previously had not received CPI therapy, with a second cohort consisting of patients that were either refractory to CPI therapy or had relapsed while on CPI therapy, meaning that no further response to CPI treatment is anticipated among patients in the second cohort. Trial participants received 200mg of pembrolizumab on day 1 of a 21-day cycle, with 0.2mg BXCL701 administered twice-daily ("BID") on days 1 through 7, the dose increasing to 0.3mg BID on Days 8 through 14. Evaluable trial participants were required to receive a minimum of two treatment cycles. A preliminary assessment of BXCL701 dosed in combination with a CPI, as of completion of the first stage, noted responses in one patient in each of the CPI naïve and CPI refractory/relapsed cohorts, including a partial response in CPI-naïve, microsatellite stable endometrial carcinoma, PD-L1 negative (CPS <1) and a partial response in CPI-refractory uveal melanoma. These preliminary results were presented at the 2021 American Society of Clinical Oncology annual meeting. Patient enrollment in this trial was completed in the third quarter of 2022.

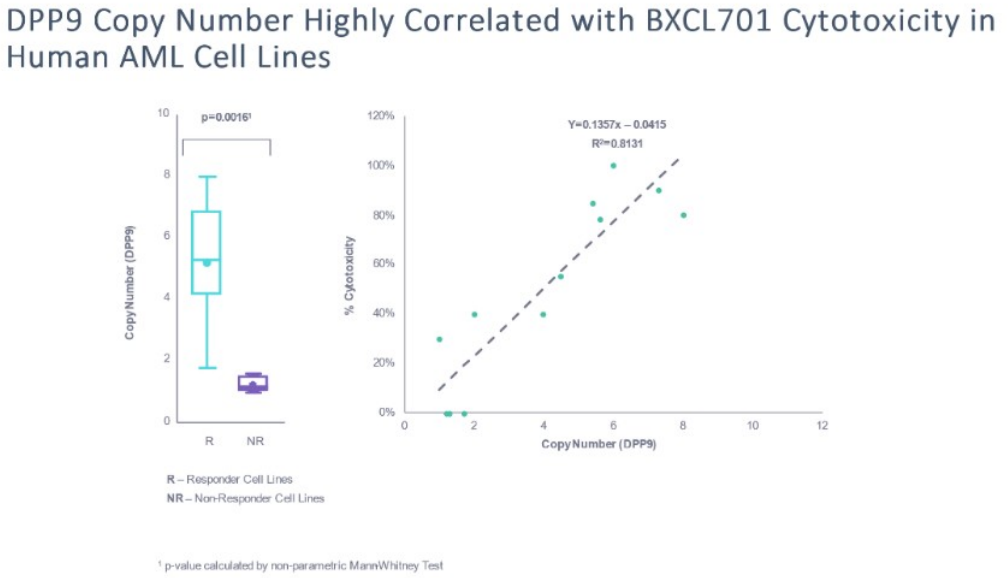
We believe BXCL701 may have potential application in breast cancer, as its use in combination with monoclonal antibody therapy generated encouraging in vivo data in a preclinical disease model where enhanced antibody-dependent cellular cytotoxicity was observed.

The FDA has granted BXCL701 orphan drug designation for the treatment of AML, stage IIb to IV melanoma, pancreatic cancer and soft tissue sarcoma. As we consider BXCL701's therapeutic potential for additional indications that represent unmet medical needs, we intend to apply for additional orphan drug designations for BXCL701.

Biomarker development initiatives intended to complement BXCL701 administration

We are also actively engaged in the identification and development of predictive biomarkers that we believe could be used in conjunction with BXCL701 to predict the likelihood of patient response to therapy across the range of targeted indications. As summarized in the preliminary data from AML patients presented below, we believe DPP9 copy number could correlate to BXCL701 response rate, with a greater likelihood of BXCL701 cytotoxicity in patients with increased DPP9 copy number. We are pursuing its use in our biomarker discovery activities as a potential companion

diagnostic. Once our current efficacy trials are completed, we plan to retrospectively analyze correlation between DPP9 copy number and response.



BXCL701 lifecycle management considerations

We envision employing computational and medicinal chemistry approaches to advance development of a next-generation BXCL701 molecule to introduce enhanced life cycle management capabilities. We anticipate that a next-generation molecule may embrace characteristics such as the simultaneous inhibition of DPP8/9 and DPP4, while providing an improved orally bioavailable pharmacokinetic profile, including a linear pharmacokinetic, a half-life of between 12 and 48 hours, with multiple mechanisms of elimination that are clearly understood and are not burdened with potential drug-drug interaction liabilities. This next generation molecule would be intended to demonstrate anti-cancer activity as either a monotherapy or in combination with an approved CPI.

Immuno-Oncology Manufacturing

We rely on third party contract manufacturing organizations to support development and manufacture of product candidates for our clinical trials, and, if any of our current or future product candidates receives marketing approval, we expect to rely on such manufacturers to meet commercial demand. We expect this strategy will enable us to maintain a more efficient infrastructure, avoiding dependence on our own manufacturing facility and equipment, while simultaneously enabling us to focus our expertise on the clinical development and future commercialization of our products. Currently, the Patheon pharma services division of Thermo Fisher Scientific Inc. and another third-party contract manufacturer supply the drug substance and clinical trial supplies for BXCL701, and we expect to enter into commercial supply agreements with such manufacturers prior to any potential approval of BXCL701.

BXCL701 drug product is manufactured via conventional pharmaceutical processing procedures, employing commercially available excipients and packaging materials. The procedure and equipment employed for manufacture and analysis are consistent with standard organic synthesis or pharmaceutical production, and are transferable to a range of manufacturing facilities, if needed. We have selected a larger third-party drug product manufacturer and will be executing technology transfer of drug product manufacture to a larger manufacturer. We also plan to maintain the current drug substance and product manufacturer as part of our supply chain strategy.

Immuno-Oncology Competition

The biotechnology and pharmaceutical industries have made substantial investments in recent years into the rapid development of novel immunotherapies for the treatment of a range of pathologies, including infectious diseases and cancers, making this a highly competitive market. We believe BXCL701 is the only innate immune system activator in clinical development specifically addressing the cold tumor problem in immuno-oncology.

We face substantial competition from multiple sources, including large and specialty pharmaceutical, biopharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions. Our competitors compete with us on the level of the technologies employed, or on the level of development of product candidates. In addition, many small biotechnology companies have formed collaborations with large, established companies to (i) obtain support for their research, development, and commercialization of products or (ii) combine several treatment approaches to develop longer lasting or more efficacious treatments that may potentially directly compete with our current or future product candidates. We anticipate that we will continue to face increasing competition as new therapies and combinations thereof, technologies, and data emerge within the field of immunotherapy and, furthermore, within the treatment of infectious diseases and cancers.

In addition to the current standard of care treatments for patients with infectious diseases or cancers, numerous commercial and academic preclinical studies and clinical trials are being undertaken by a large number of parties to assess novel technologies and product candidates in the field of immunotherapy. Results from these studies and trials have fueled increasing levels of interest in the field of immunotherapy.

Large pharmaceutical companies that have commercialized or are developing immunotherapies to treat cancer include AstraZeneca AB, Bristol-Myers Squibb Company, Merck & Co., Inc., Novartis AG, Pfizer Inc. and F. Hoffmann-La Roche Ltd.

We face significant competition from pharmaceutical and biotechnology companies that target specific tumor-associated antigens using immune cells or other cytotoxic modalities. These generally include immune cell redirecting therapeutics such as T cell engagers, adoptive cellular therapies such as CAR-Ts, antibody drug conjugates, targeted radiopharmaceuticals, targeted immunotoxin, and targeted cancer vaccines.

Clinical stage companies that compete with us directly on the level of the development of product candidates targeting the innate immune system include Amgen Inc., Mirati Therapeutics, Inc., Bristol- Myers Squibb Company, Ryvu Therapeutics, Merck & Co., Inc., Replimune Group Inc., Nektar Therapeutics, Novartis AG, Xbiotech Inc., Stingthera, Inc., AstraZeneca AB, F. Hoffmann-La Roche Ltd and Aravive, Inc. Clinical stage companies that compete with us directly on the level of the development of product candidates targeting the mCRPC include Astellas Pharma Inc., Pfizer Inc., Bayer AG, Janssen, Sanofi S.A., Clovis Oncology, Inc., AstraZeneca AB, Merck & Co., Inc., GSK plc, Tempest Therapeutics, Inc., Zenith Epigenetics Ltd. and Gossamer Bio, Inc. Clinical stage companies that compete with us directly on the level of the development of product candidates utilizing the therapeutic potential of synthetic lethality include Repare Therapeutics Inc., IDEAYA Biosciences, Inc. and Tango Therapeutics, Inc.

Many of our competitors, either alone or in combination with their respective strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, the regulatory approval process, and marketing than we do. Mergers and acquisition activity in the pharmaceutical, biopharmaceutical and biotechnology sector is likely to result in greater resource concentration among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through sizeable collaborative arrangements with established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if one or more of our competitors develop and commercialize products that are safer, more effective, better tolerated, or of greater convenience or economic benefit than our proposed product offerings. Our competitors also may be in a position to obtain FDA or other regulatory approval for their products more rapidly, resulting in a stronger or dominant market position before we are able to enter

the market. The key competitive factors affecting the success of all of our programs are likely to be product safety, efficacy, convenience and treatment cost.

Immuno-Oncology Intellectual Property

Intellectual property is of vital importance in our field and in biotechnology generally. We seek to protect and enhance proprietary technology, inventions, and improvements that are commercially important to the development of our business by seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We will also seek to rely on regulatory protection afforded through inclusion in expedited development and review, data exclusivity, market exclusivity, and patent term extensions where available.

As of January 31, 2023, we have multiple patent families filed to protect our Immuno-Oncology portfolio, including our core patent family directed to methods of using BXCL701 with immune checkpoint inhibitors, which has granted/allowed patents in the U.S., Japan, Australia, Canada, Russia, China, Mexico, and South Africa, with pending applications in the U.S., Mexico, the Republic of Korea, the UAE, New Zealand, Russia, Australia, Brazil, Hong Kong, and Europe. Patents issuing from this family are expected to expire no earlier than 2036.

Our current immuno-oncology portfolio includes one issued utility patent in the U.S., one in Japan, eight in other countries, as well as seven pending utility patent applications in the U.S. including one received Notice of Allowance, 35 pending non-U.S. utility patent applications, and five pending U.S. provisional applications directed to novel formulations of BXCL701, various dosing regimens, methods of use, biomarker, and combination therapies. We expect that those issued/granted patents and patents issuing from these applications, if any, will expire from 2039 to 2043.

We expect to file additional patent applications in support of current and new immuno-oncology clinical candidates as well as new platform and core technologies. For additional information regarding intellectual property regulations and risks, see above under “—Neuroscience—Neuroscience Intellectual Property” and Part I, Item 1A, “Risk Factors - Risks Related to Our Intellectual Property.”

Our Relationship with BioXcel LLC

BioXcel LLC currently holds an ownership interest of approximately 30% in the Company and our pipeline compounds were identified by applying our growing internal AI capabilities, along with BioXcel LLC’s EvolverAI, a proprietary pharmaceutical discovery and development engine, for drug re-innovation.

We entered into the Amended and Restated Asset Contribution Agreement (the “Contribution Agreement”), pursuant to which BioXcel LLC, agreed to contribute BioXcel LLC’s rights, title and interest in BXCL501, BXCL701, BXCL502 and BXCL702, and all of the assets and liabilities associated in consideration for (i) 9,480,000 shares of our common stock, (ii) $1 million upon completion of an initial public offering, (iii) $500,000 upon the later of the 12 month anniversary of an initial public offering and the first dosing of a patient in the bridging bioavailability/bioequivalence study for the BXCL501 program, (iv) $500,000 upon the later of the 12 month anniversary of an initial public offering and the first dosing of a patient in the Phase 2 proof of concept open-label monotherapy or combination trial with Keytruda for the BXCL701 program and (v) a one-time payment of $5 million within 60 days after the achievement of $50 million in cumulative net sales of any product or combination of products resulting from the development and commercialization of any one of the contributed product candidates or a product derived therefrom. As of December 31, 2022, all of the foregoing have been paid except for (v).

We entered into a Separation and Shared Services Agreement with BioXcel LLC that took effect on June 30, 2017, as amended and restated thereafter (the “Services Agreement”), pursuant to which services provided by BioXcel LLC through its subsidiaries in India and the U.S. will continue indefinitely, as agreed upon by the parties. These services are primarily for drug discovery, chemical, manufacturing and controls (“CMC”) cost and general and administrative support. The Company has an option, exercisable until December 31, 2024, to enter into a collaborative services agreement with BioXcel LLC pursuant to which BioXcel LLC shall perform product identification and related services for us utilizing EvolverAI, its proprietary pharmaceutical discovery and development engine. To maintain the ability to exercise the foregoing option, pursuant to an amendment to the Services Agreement effective as of April 19, 2022, the Company has agreed to pay BioXcel LLC $18,000 per month from March 13, 2023 to December 31, 2024. The parties

are obligated to negotiate the collaborative services agreement in good faith and to incorporate reasonable market-based terms, including consideration for BioXcel LLC reflecting a low, single-digit royalty on net sales and reasonable development and commercialization milestone payments, provided that (i) development milestone payments shall not exceed $10 million in the aggregate and not be payable prior to proof of concept in humans and (ii) commercialization milestone payments shall be based on reaching annual net sales levels, be limited to 3% of the applicable net sales level, and not exceed $30 million in the aggregate.

Service charges recorded under the Services Agreement were $1.4 million for each of the years ended December 31, 2022 and 2021.

Government Regulation

Government Regulation and Product Approval

Government authorities in the U.S., 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 NDA process before it may be legally marketed in the U.S. 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 U.S. federal, state, and local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Drug Development Process

In the U.S., the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (“FDCA”), and its implementing regulations. The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA’s Good Laboratory Practice 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 clinical 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 clinical 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 facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice (“cGMP”) requirements to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity, and potential inspection 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 specified indications for use in the U.S.

Prior to beginning the first clinical trial with a product candidate in the U.S., 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 any clinical trials can begin. Submission of an IND 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. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and its investigators for actual or suspected serious and adverse events, along with any findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs and findings from animal or in vitro testing suggesting a significant risk to humans, as well as any clinically important increased incidence of a suspected serious adverse reaction compared to that listed in the protocol or investigator brochure.

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 a study can move forward at designated check points, based on access to data from the study, and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other for other grounds, such as no demonstration of efficacy. 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 companies 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.

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.

In addition, during the development of a drug, sponsors are given opportunities to periodically meet with or seek feedback from the FDA. These interactions may be requested, for example, prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. These interactions 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 alignment 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 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 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, and of ten months from the date of NDA receipt to complete a standard review of an NDA for a drug that is not a new molecular entity.

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 review, evaluate and provide a recommendation as to whether the NDA 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 comply with cGMP and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs.

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 and sale of the product with specific prescribing information for specific indications. A CRL will describe the deficiencies that the FDA identified in the NDA, except that in those instances where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting any 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 specific 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, such as restricted distribution methods, patient registries, and other risk minimization tools. 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, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Regulation of Combination Products in the U.S.

Certain products are comprised of components, such as drug components and device components, which would normally be subject to different regulatory frameworks by the FDA and frequently regulated by different centers at the FDA. These products are known as combination products. Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug-device combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established the Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

A combination product with a primary mode of action attributable to the drug component generally would be reviewed and approved pursuant to the drug approval processes set forth in the FDCA. In reviewing the NDA for such a product, however, FDA reviewers would consult with their counterparts in the device center to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the Quality System Regulations ("QSR") applicable to medical devices.

Expedited Development and Review Programs

The FDA offers 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 product candidates 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 candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the NDA may be eligible for priority review. An NDA for a Fast Track product candidate 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 Breakthrough Therapy designation includes 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 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 FDA review programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. An NDA is eligible for priority review if the product candidate 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 application within six months of the 60-day filing date, or with respect to non-new-molecular-entity NDAs, within six months of the NDA receipt 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. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the relevant product.

Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval do not change the standards for approval, but such designations 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 to qualify for such program or may 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 U.S., or a

patient population greater than 200,000 individuals in the U.S. and when there is no reasonable expectation that the cost of developing and making available the drug in the U.S. will be recovered from sales in the U.S. 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 a particular active ingredient for the disease 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 disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. 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 benefits of orphan drug designation are tax credits for certain research costs and a waiver of the NDA 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 U.S. 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 events, 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 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. 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. 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 health care 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.

Hatch-Waxman Act

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application ("ANDA"). An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. ANDAs are termed "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's drug or a method of using the drug. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

Upon submission of an ANDA or a 505(b)(2) NDA, an applicant must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification (a "paragraph IV certification"). If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired. If the ANDA or 505(b)(2) NDA applicant has provided a paragraph IV certification to the FDA, the applicant

must send notice of the paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. If the paragraph IV certification is challenged by an NDA holder or the patent owner(s) asserts a patent challenge to the paragraph IV certification, the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation.

The Hatch-Waxman Act establishes periods of regulatory exclusivity for certain approved drug products, during which the FDA cannot approve (or in some cases accept) an ANDA or 505(b)(2) application that relies on the branded reference drug. For example, the holder of an NDA, including a 505(b)(2) NDA, may obtain five years of non-patent data exclusivity upon approval of a new drug containing new chemical entities that have not been previously approved by the FDA. 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 therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The Hatch-Waxman Act also provides three years of marketing exclusivity to the holder of an NDA (including a 505(b)(2) NDA) for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted or sponsored by the applicant. This three-year exclusivity period protects against FDA approval of ANDAs and 505(b)(2) NDAs for the condition of the new drug's approval. As a general matter, the three year exclusivity does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. 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 efficacy.

FDA Approval and Regulation of Medical Devices and Companion Diagnostics

If safe and effective use of a therapeutic depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of in vitro companion diagnostics in conjunction with the review of our product candidates in development for cancer will, therefore, likely involve coordination of review by the FDA’s Center for Drug Evaluation and Research and the FDA’s Center for Devices and Radiological Health Office of In Vitro Diagnostics and Radiological Health.

Under the FDCA, in vitro diagnostics, including companion diagnostics, are regulated as medical devices. In the U.S., the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, medical devices, including companion diagnostic tests, require marketing clearance or approval from the FDA prior to commercial distribution.

The two primary types of FDA marketing authorization applicable to a medical device are premarket notification ("510(k) clearance") and premarket approval ("PMA"). To obtain 510(k) clearance, a manufacturer must submit to the FDA a premarket notification submission demonstrating that the proposed device is "substantially equivalent" to a legally marketed predicate device. The FDA's 510(k) clearance process usually takes from three to twelve months but may take longer. The FDA may require additional information, including clinical data, to make a determination regarding substantial equivalence. If the FDA agrees that the device is substantially equivalent to a predicate device currently on the market, it will grant 510(k) clearance to commercially market the device. If the FDA determines that the device is "not substantially equivalent" to a previously cleared device, the device is automatically designated as a Class III (i.e., high-risk) device. The device sponsor must then fulfill more rigorous PMA requirements or can request a risk-based classification determination for the device in accordance with the "de novo" process, which is a route to market for novel medical devices that are low to moderate risk and are not substantially equivalent to a predicate device.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a major change or modification in its intended use, will require a new 510(k) clearance or depending on the modification, approval of a PMA application or de novo classification. The FDA requires each manufacturer to determine whether the proposed change requires submission of a 510(k), de novo classification or a PMA in the first instance, but the FDA can review any such decision and disagree with a manufacturer's determination. If the FDA disagrees with a manufacturer's determination, the FDA can require the manufacturer to cease marketing and/or request the recall of the modified device until it receives 510(k) clearance, approval of a PMA application, or issuance of a de novo classification. Also, in these circumstances, the manufacturer may be subject to significant regulatory fines or penalties.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the QSR which imposes elaborate testing, control, documentation and other quality assurance requirements.

Approval of a PMA is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained, or problems are identified following initial marketing.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and

shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the U.S.

International Regulations

In addition to regulations in the U.S., we are and will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials, marketing authorization, post-marketing requirements and any commercial sales and distribution of our products. We must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of any products in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-Clinical Studies and Clinical Trials

Similar to the U.S., the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice ("GLP") as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization ("ICH") guidelines on Good Clinical Practices ("GCP") as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB, respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally,

sponsors could choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those are governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

During the development of a medicinal product, the EMA and national regulators provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use ("CHMP"). A fee is incurred with each scientific advice procedure. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical trials, and pharmacovigilance plans and risk-management programs. Advice is not legally binding to any future marketing authorization ("MA") application ("MAA") of the product concerned.

Marketing Authorization

In order to market our product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal products candidates can only be placed on the market after obtaining a MA. To obtain regulatory approval of a product candidate in the EU, we must submit a MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MA": are issued by the European Commission through the centralized procedure based on the opinion of the EMA's CHMP and are valid throughout the EU. The centralized procedure is compulsory for certain types of medicinal products such as (i) medicinal products derived from biotechnology processes, such as genetic engineering, (ii) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV or AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) designated orphan medicinal products, and (iv) advanced therapy medicinal products ("ATMPs") such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- "National MA": are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the Centralized MAs. Where a product has already been authorized for marketing in an EU member state, this National MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a National MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure, an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the Centralized MA, the maximum timeframe for the evaluation of a MAA by the EMA is 210 days. This excludes so-called clock stops, during which additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. At the end of the review period, the CHMP provides an opinion to the European Commission. If this opinion is favorable, the European Commission may then adopt a decision to grant an MA. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme, facilitating increased understanding of the product at EMA's committee level. An

initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the European Commission or the national competent authority decides on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal.

Data and Marketing Exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving a MA, reference product generally receives eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the U.S. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition.

The application for orphan drug designation must be submitted before the MAA. Orphan designation entitles a party to incentives such fee reductions or fee waivers, protocol assistance, and access to the Centralized MA process. Upon grant of a MA, orphan medicinal products are entitled to 10 years of market exclusivity for the approved therapeutic indication. During the 10-year market exclusivity period, the competent authorities cannot accept a MAA, or grant a MA, or accept an application to extend a MA, for the same indication, in respect of a similar medicinal product. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan ("PIP"). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, a MA may be granted to a similar product for the same indication at any time if (1) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (2) the applicant consents to a second orphan medicinal product application; or (3) the applicant cannot supply enough orphan medicinal product.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product

seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the European Economic Area ("EEA") which consists of the 27 EU member states plus Iceland, Liechtenstein, Norway, Switzerland and Turkey, as well as cooperating countries Albania, Bosnia and Herzegovina, Kosovo, Montenegro, North Macedonia and Serbia.

The United Kingdom ("UK") left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement ("TCA") and became effective on January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of Good Manufacturing Practice ("GMP") inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

Other Foreign Regulations

For other countries outside of Europe, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Regulation of Companion Diagnostics

In the EU, in vitro diagnostic medical devices are regulated by Directive 98/79/EC which regulates the placing on the market, the CE marking, the essential requirements, the conformity assessment procedures, the registration obligations for manufacturers and devices, as well as the vigilance procedure. In vitro diagnostic medical devices must comply with the requirements provided for in the Directive, and with further requirements implemented at national level (as the case may be).

The regulation of companion diagnostics is subject to requirements of the in-vitro medical diagnostic devices Regulation (No 2017/746) ("IVDR"). The IVDR was fully effective May 26, 2022, but there is a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation.

The IVDR introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the Centralized MA process for the authorization of medicines, or the medicinal product is already authorized through the Centralized MA process, or a MAA for the medicinal product has been submitted through the Centralized MA process. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA.

The aforementioned EU rules are generally applicable in the EEA.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of drug products for which we obtain regulatory approval. In the U.S. and other countries, sales of products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, new products are facing increasingly high barriers to entry. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the U.S. has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is secured for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

To raise sufficient financial resources to commercialize our approved products and continue to advance our product candidates, we will need to address pricing pressures and potential third-party reimbursement coverage for our approved products and product candidates. In the U.S. and elsewhere, sales of pharmaceutical products depend in significant part on the availability of reimbursement to the consumer from third-party payors, such as government and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. It is and will continue to be time consuming and expensive for us or our strategic collaborators to go through the process of seeking reimbursement from Medicare and private payors. Our products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

Healthcare Reform

We participate in the Medicaid Drug Rebate Program and other federal and state government pricing programs in the U.S., and we may participate in additional government pricing programs in the future. The U.S. government and other governments have shown significant interest in pursuing health care reform, which has resulted in changes to these programs and impacts IGALMI and our product candidates that may be approved. For example, in March 2010, the Patient Protection and Affordable Care Act ("ACA"), as amended by the Health Care and Education Reconciliation Act,

was enacted and this health care reform law substantially changed the way health care is financed in the U.S. by both government and private insurers. Among other cost containment measures, the ACA established:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents;
- a Medicare Part D coverage gap discount program, in which pharmaceutical manufacturers who wish to have their drugs covered under Part D must offer discounts to eligible beneficiaries during their coverage gap period, or the "donut hole"; and
- a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program.

Since its enactment, there have been judicial, executive and congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the U.S. Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to health care, 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. In addition, we expect that federal, state and local governments in the U.S. will continue to consider legislation to limit the growth of health care costs, including the cost of prescription drugs. Future legislation could limit payments for pharmaceuticals such as IGALMI and the product candidates that we are developing.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers, which will remain in effect through 2032 with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, absent additional congressional action. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, in March 2021, Congress enacted the American Rescue Plan Act of 2021, which, among other things, eliminated the statutory cap on drug manufacturers' Medicaid Drug Rebate Program rebate liability, effective January 1, 2024.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. In addition, individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical 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, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

Future legislation could limit payments for pharmaceuticals such as IGALMI and the product candidates that we are developing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressures. The implementation of cost containment

measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Other Health Care Laws and Compliance Requirements

For approved products, we may be subject to various federal, state and foreign laws targeting fraud and abuse in the health care industry. Such laws include, without limitation, U.S. federal and state anti-kickback, fraud and abuse, false claims, consumer fraud, and transparency laws and regulations with respect to drug pricing and payments and other transfers of value made to physicians and other health care professionals, as well as similar foreign laws in jurisdictions outside the U.S.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal health care program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for health care items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The federal False Claims Act imposes liability on any person who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal health care program. 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 False Claims Act. The “qui tam” provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payer and not merely a federal health care program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus significant civil penalties for each separate false claim.

Also, the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), created several federal crimes, including health care fraud, and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private third-party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation.

The Physician Payment Sunshine Act (the “Sunshine Act”), which was enacted as part of the ACA, requires applicable manufacturers of drugs, devices, biologicals, or medical supplies covered under Medicare, Medicaid or the Children’s Health Insurance Program, to report annually to the Secretary of the Department of Health and Human Services payments or other transfers of value made by that entity, or by a third-party as directed by that entity, to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers including physician assistants and nurse practitioners, and teaching hospitals, or to third parties on behalf of such providers, as well as ownership and investment interests held by physicians and their immediate family members during the course of the preceding calendar year. Failure to comply with the reporting requirements can result in significant civil monetary penalties for any payment or other transfer of value that is not reported.

Moreover, analogous state and foreign laws and regulations may be broader in scope than the provisions described above and may apply regardless of payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and relevant federal government compliance guidance; require drug manufacturers to report information related to payments and other transfers of value to physicians and other health care providers, many of which differ from each other in significant ways, thus further complicating compliance efforts; and restrict marketing practices or require disclosure of marketing expenditures and pricing information.

Violations of any of these laws or any other governmental laws and regulations that may apply include, without limitation, significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded health care programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

Data Privacy & Security

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the U.S., numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, including HIPAA, and federal and state consumer protection laws and regulations (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, certain state and non-U.S. laws, such as the California Consumer Privacy Act ("CCPA"), the California Privacy Rights Act ("CPRA"), and the EU General Data Protection Regulation ("GDPR"), govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing. Additionally, our use of AI and machine learning may be subject to laws and evolving regulations regarding the use of AI or machine learning, controlling for data bias, and anti-discrimination.

Human Capital

Our Employees

We grew our overall headcount over 100% compared to last year to a team of 183 full-time employees as of December 31, 2022. The headcount increases in 2022 were primarily related to building out our commercial team, as well as adding employees in general and administrative functions to support the growth of our business and commercialization of IGALMI. We also leverage certain experts in drug development and AI that are employed by BioXcel LLC to provide flexibility for our business needs.

We expect to continue to hire additional employees in 2023 as we expand our commercialization and increase our clinical and preclinical efforts.

Our Culture

We believe that the success of our human capital management investments is evidenced by our low employee turnover, a number which is regularly reviewed by our Board of Directors as part of their oversight of our human capital strategy.

Employee Engagement, Talent Development & Benefits

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries, bonuses, opportunities for equity ownership and other comparable benefits for our industry.

Employee and Visitor Safety Protocols

The Company follows health and safety guidelines to protect the well-being of our employees and visitors.

Diversity & Inclusion

Much of our success is rooted in the diversity of our teams and our commitment to inclusion. We value diversity at all levels and continue to focus on extending our diversity and inclusion initiatives across our entire workforce. We believe that our business benefits from the different perspectives a diverse workforce brings, and we pride ourselves on having a strong, inclusive and positive culture based on our shared mission and values.

Our Corporate Information

The Company was incorporated as a Delaware corporation on March 29, 2017. Our principal executive offices are located at 555 Long Wharf Drive, New Haven, CT 06511 and our telephone number is (475) 238-6837.

Available Information

Our website address is www.bioxceltherapeutics.com. The contents of, or information accessible through, our website are not part of this Annual Report on Form 10-K. We make our filings with the SEC, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports, available free of charge on our website as soon as reasonably practicable after we file such reports with, or furnish such reports to, the SEC.

We may use our website as a distribution channel of material information about the Company. Financial and other important information regarding the Company is routinely posted on and accessible through the Investors & Media sections of our website at www.bioxceltherapeutics.com. In addition, you may automatically receive email alerts and other information about the Company when you enroll your email address by visiting the “Email Alerts” option under the News / Events menu of the Investors & Media section of our website at www.bioxceltherapeutics.com.

The reference to our website address does not constitute incorporation by reference of the information contained on or available through our website, and you should not consider such information to be a part of this Annual Report on Form 10-K.

Item 1A. Risk Factors

You should carefully consider the risks described below, as well as general economic and business risks and the other information in this Annual Report on Form 10-K. The occurrence of any of the events or circumstances described below or other adverse events could have a material adverse effect on our business, results of operations and financial condition and could cause the trading price of our common stock to decline. Additional risks or uncertainties not presently known to us or that we currently deem immaterial may also harm our business.

Risks Related to Financial Position and Need for Additional Capital

We have a limited operating history and have not generated substantial product revenues to date, which may make it difficult to evaluate the success of our business and to assess our future viability.

We were incorporated in March 2017 and our operations to date have been largely focused on staffing our company, raising capital, advancing the development of our product candidates, including conducting clinical and preclinical studies and establishing our commercial organization. We have only one product approved for commercial sale, and have limited experience in obtaining marketing approvals, manufacturing products on a commercial scale, and conducting sales and marketing activities necessary for successful commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully commercializing products.

We expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. We are transitioning from a company with primarily a research and development focus to a company also capable of undertaking commercial activities. We may encounter unforeseen expenses, difficulties, complications, and delays, and may not be successful in such a transition.

We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.

Since our inception, we have incurred significant operating losses. Our net loss was $165.8 million and $106.9 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had stockholders' equity of $76.8 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We have only one product candidate approved for marketing in the U.S., none in any other jurisdiction, and may never receive approval beyond the one product approved to date. It could be several years, if ever, before we have a commercialized product that generates significant revenues through sales of IGALMI or our product candidates, if approved. As a result, we are uncertain when or if we will achieve profitability and, if so, whether we will be able to sustain it. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue the development of our product candidates;
- conduct preclinical studies and clinical trials for our current product candidates and any future product candidates that we may pursue;
- continue to build our portfolio of product candidates through the acquisition or in-license of additional product candidates or technologies;
- continue to develop, maintain, expand and protect our intellectual property portfolio;
- pursue regulatory approvals for our current and future product candidates that successfully complete clinical trials;
- fully develop a sales, marketing, and distribution infrastructure to commercialize IGALMI and any other product candidates for which we may obtain marketing approval;
- hire additional clinical, commercial, regulatory, scientific and finance personnel; and

- incur additional legal, accounting and other expenses in operating as a public company.

To become and remain profitable, we must develop and eventually commercialize one or more products or product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing clinical trials of our product candidates, developing commercial scale manufacturing processes, obtaining marketing approval, manufacturing, marketing, and selling IGALMI and any current and future product candidates for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in any, or all, of these activities and, even if we do, we may never generate sufficient revenue to achieve profitability.

Although we have obtained FDA approval for IGALMI, because of the numerous risks and uncertainties associated with product development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will obtain marketing approval to commercialize any additional product candidates. If we are required by the FDA, or other regulatory authorities such as the EMA to perform studies and trials in addition to those currently expected, or if there are any delays in the development, or in the completion of any planned or future preclinical studies or clinical trials of our current or future product candidates, our expenses could increase, and profitability could be further delayed.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable would decrease the value of our Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations. A decline in the value of our Company also could cause you to lose all or part of your investment.

We will need substantial additional funding and, if we are unable to raise capital when needed, we could be forced to delay, reduce, or eliminate our product development programs or commercialization efforts.

We anticipate that our expenses will increase substantially if and as we continue to develop and conduct clinical trials with respect to our current and any future product candidates; seek to identify and develop additional product candidates; acquire or in-license other product candidates or technologies; seek regulatory approvals for our product candidates that successfully complete clinical trials, if any; establish sales, marketing, distribution and other commercial infrastructure to support the commercialization of products for which we may obtain marketing approval; require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization; maintain, expand and protect our intellectual property portfolio; hire and retain additional personnel, such as clinical, quality control and scientific personnel; add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and add equipment and physical infrastructure to support our research and development programs.

We expect that our cash and cash equivalents as of December 31, 2022, will be sufficient to fund our ongoing research and development efforts and commercialization efforts for at least twelve months from the date of the issuance of the consolidated financial statements included in this Annual Report on Form 10-K. We will be required to expend significant funds to commercialize IGALMI in the U.S. and advance the development of BXCL501, BXCL701, BXCL502 and our other product candidates. In addition, while we may seek one or more collaborators for future development of our current product candidates or any future product candidates that we may develop for one or more indications, we may not be able to enter into a collaboration for any of our product candidates for such indications on suitable terms, on a timely basis or at all. In any event, our existing cash will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of our product candidates or our other preclinical programs. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We may also seek third-party investments in or other strategic options for our subsidiary, OnkosXcel. Further financing may not be available to us on acceptable terms, or at all. In addition, we are reliant on the financial institutions with which we hold our cash and cash equivalents. If such institutions were to close, we may not be able to recover all of our cash or cash equivalents held at such institutions. Moreover, market volatility resulting from the COVID-19 pandemic, credit crises, adverse macroeconomic conditions, such as high interest or inflation rates, or other factors could also adversely impact our ability to access capital as and

when needed. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

The Company maintains its cash and cash equivalents in accounts with major U.S. and multi-national financial institutions, and our deposits at several of these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, we could lose our deposits in excess of the federally insured or protected amounts and there can be no assurance that we will be able to access uninsured funds in a timely manner or at all.

Our estimate as to how long we expect our existing cash 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. Further, 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. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs, and results of clinical trials of our product candidates;
- our ability to enter into and the terms and timing of any collaborations, licensing agreements or other arrangements;
- the costs, timing and outcome of seeking regulatory approvals;
- the costs of commercialization activities for IGALMI and for any of our product candidates that receive marketing approval, to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- revenue received from commercial sales of IGALMI and our current and future product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the number of future product candidates that we pursue and their development requirements;
- changes in regulatory policies or laws that may affect our operations;
- changes in physician acceptance or medical society recommendations that may affect commercial efforts;
- the costs of acquiring potential new product candidates or technology;
- the costs of operating as a public company; and
- costs associated with any adverse market conditions or other macroeconomic factors.

We have significant indebtedness and other contractual obligations that could impair our liquidity, restrict our ability to do business and thereby harm our business, results of operations and financial condition. We may not have sufficient cash flow from operations to satisfy our obligations under the OFA Facilities.

As of March 13, 2023, we had aggregate principal indebtedness of $100.8 million outstanding under two strategic financing agreements: a Credit Agreement and Guaranty (the “Credit Agreement”) by and among the Company, as the borrower, certain subsidiaries of the Company from time to time party thereto as subsidiary guarantors, the lenders party thereto (the “Lenders”), and Oaktree Fund Administration LLC (“OFA”) as administrative agent, and a Revenue Interest Financing Agreement (the “RIFA”; and together with the Credit Agreement, the “OFA Facilities”) by and among the Company, the purchasers party thereto (the “Purchasers”) and OFA as administrative agent. Approximately $70.8

million of the indebtedness relates to the Credit Agreement, pursuant to which the Lenders have agreed to loan us up to an additional $65.0 million in senior secured term loans, and $30.0 million relates to the RIFA, pursuant to which the Purchasers agreed to fund an additional $90.0 million upon satisfaction of certain conditions. The RIFA requires us to make tiered revenue interest payments on U.S. net sales of IGALMI and any other future BXCL501 products equal to a royalty ranging from 0.375% to 7.750% of net sales of IGALMI and any other future BXCL501 products in the U.S., as well as certain additional payments to the Purchasers from time to time, to ensure that the aggregate amount of payments received by the Purchasers under the RIFA are at least equal to certain agreed upon minimum levels as of certain specified dates, subject to terms and conditions set forth in the RIFA.

Our ability to make scheduled payments or to refinance these and other outstanding debt obligations depends on our financial and operating performance, which will be affected by prevailing economic, industry and competitive conditions and by financial, business and other factors beyond our control. A failure to pay our debt, fixed costs and other obligations or a breach of our contractual obligations could result in a variety of adverse consequences, including the acceleration of our obligations or the exercise of remedies by our creditors and lessors. In such a situation, it is unlikely that we would be able to cure our breach, fulfill our obligations, make required payments, or otherwise cover our fixed costs, which would have a material adverse effect on our business, results of operations and financial condition.

In addition, historically we have relied on debt and equity financings as our primary sources of liquidity. If our future cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay capital expenditures, sell assets, seek additional capital or seek to restructure or refinance our indebtedness. Any refinancing of our indebtedness could be at higher interest rates and may require us to comply with more onerous covenants. These alternative measures may not be successful and may not permit us to meet our scheduled debt service obligations. In the absence of such cash flows and resources, we could face substantial liquidity problems and might be required to sell material assets or operations to attempt to meet our debt service obligations. If we cannot meet our debt service obligations, the holders of our indebtedness may accelerate such indebtedness and, to the extent such indebtedness is secured, foreclose on our assets. In such an event, we may not have sufficient assets to repay all of our indebtedness.

In addition, incurring indebtedness generally requires that a portion of cash flow from operating activities be dedicated to interest and principal payments. Debt service requirements could reduce our ability to use our cash flow to fund operations and capital expenditures, to capitalize on future business opportunities, including additional acquisitions, or to pay dividends or increase dividends. In addition, our indebtedness may reduce our flexibility to operate our business, adjust to changing business conditions, restrict us from making strategic acquisitions or cause us to make non-strategic divestitures or obtain additional financing. Any of these risks could materially adversely affect our business, results of operations or financial condition.

Restrictive covenants in the Credit Agreement and RIFA each place limits on our ability to conduct our business. The Credit Agreement contains customary representations and warranties and customary affirmative and negative covenants, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of other indebtedness, and dividends and other distributions, subject to certain exceptions, including specific exceptions with respect to product commercialization and development activities. We must also comply with certain financial covenants under the Credit Agreement that require we maintain a minimum cash liquidity amount of $15 million and future revenue thresholds beginning in with the fourth quarter of 2023. The RIFA contains customary representations and warranties and certain restrictions on our ability to incur indebtedness and grant liens on intellectual property related to BXCL501. In addition, the RIFA provides that if certain events occur, including certain bankruptcy events, failure to make payments, a change of control, an out-license or sale of all of the rights in and to BXCL501 in the U.S., in each case except a permitted licensing transaction (as defined in the RIFA) and, subject to applicable cure periods, material breach of the covenants in the RIFA, OFA, at the direction of the Purchasers, may require us to repurchase certain of the Purchasers' interests.

Risks Related to the Discovery and Development of Product Candidates

We have limited experience in drug discovery and drug development.

Prior to the acquisition of our product and product candidates, we were not involved in and had no control over their preclinical and clinical development. In addition, we are relying upon the parties we acquired our product candidates from to have conducted research and development in accordance with the applicable protocol, legal, regulatory and scientific standards, accurately reported the results of all clinical trials conducted prior to our acquisition of the applicable product candidate, and correctly collected and interpreted the data from these studies and trials. To the extent any of these activities did not occur, our expected development time and costs could increase, which could adversely affect our prospects for marketing approval of, and receiving any future revenue from, these product candidates.

In the near term, we are dependent on the success of IGALMI, and four of our product candidates, BXCL501, BXCL502, BXCL701 and BXCL702. If we are unable to complete the clinical development of or obtain marketing approval for our product candidates or successfully commercialize IGALMI and our other product candidates, either alone or with a collaborator, or if we experience significant delays in doing so, our business could be substantially harmed.

We currently have only one product that has received regulatory approval and may never be able to develop additional marketable product candidates. We are continuing to invest a significant portion of our efforts and financial resources in the commercialization of IGALMI and development of BXCL501, BXCL502, BXCL701 and BXCL702, as well as our other product candidates. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize product candidates in one or more disease indications.

The success of IGALMI, and of BXCL501, BXCL701, BXCL502 and our other product candidates will depend on several factors, including the following:

- acceptance of an IND by the FDA or acceptance of comparable applications by foreign regulatory authorities allowing us to conduct clinical trials of our product candidates in the U.S. or in foreign jurisdictions;
- initiation, progress, timing, costs and results of clinical trials of our product candidates and potential product candidates;
- demonstration of safety and efficacy of our product candidates to the satisfaction of the FDA, or any comparable foreign regulatory authority, and sufficient for marketing approval;
- the timing and performance of our current and future collaborators;
- the nature of any required post-marketing clinical trials or other commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- establishment of arrangements with third-party manufacturers to obtain finished drug product that is appropriately packaged for sale;
- adequate ongoing availability of raw materials and drug product for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the U.S. and internationally;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;

- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including the results of clinical trials, the time required for the FDA, or any comparable foreign regulatory authorities, to review any regulatory submissions we may make, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to commercialize IGALMI or develop, receive marketing approval for and successfully commercialize BXCL501, BXCL701 and our other product candidates, on our own or with any future collaborator, or experience delays because of any of these factors or otherwise, our business could be substantially harmed.

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 may publicly disclose top-line or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data. The results and related findings and conclusions based on such preliminary data are subject to change, and have in the past changed, 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 or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, top-line and preliminary 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. Adverse differences between interim data and final data could significantly harm 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 harmed, which could harm our business, operating results, prospects, or financial condition.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, expensive and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. It is not uncommon for companies in the biopharmaceutical industry to suffer significant

setbacks in advanced clinical trials due to nonclinical findings made while clinical studies are underway and safety or efficacy observations made in clinical studies, including previously unreported adverse events. Our future clinical trial results may not be successful, and notwithstanding any potential promising results in earlier studies, we cannot be certain that we will not face similar setbacks. The historical failure rate for product candidates in our industry is high. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during a product candidate's clinical development and may vary among jurisdictions. We obtained regulatory approval for our first product candidate for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder, which has not yet been successfully commercialized. It is possible that none of our other product candidates, or any product candidates we may seek to develop in the future, will ever obtain regulatory approval.

Our current product candidates, or any that may be developed in the future, could 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;
- 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;
- 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 U.S. or elsewhere;
- the FDA, or comparable foreign regulatory authorities, may disagree that our changes to branded reference drugs meet the criteria for the 505(b)(2) regulatory pathway or comparable foreign regulatory pathways;
- the FDA, or comparable foreign regulatory authorities, may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; 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.

We have limited experience in completing clinical trials of product candidates. Consequently, we may not have the necessary capabilities, including adequate staffing, to successfully manage the execution and completion of clinical trials we initiate in a way that leads to our obtaining marketing approval for our product candidates in a timely manner, or at all. This 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 significantly harm our business, results of operations, and prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, 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 or may restrict its distribution. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

We have only submitted one NDA to the FDA and have not submitted any similar marketing applications to comparable foreign authorities, for any product candidate, and we cannot be certain that our product candidates currently in development, or any than may be developed in the future, will be successful in clinical trials or receive regulatory approval. Further, our product candidates currently in development, or any than may be developed in the future, may not

receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for additional product candidates, we may not be able to continue our operations. For any regulatory approvals to market one or more of our product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patients that we are targeting for IGALMI or our other product candidates are not as significant as we estimate, we may not generate significant revenues from sales of IGALMI or such other product candidates, if approved.

We plan to seek regulatory approval to commercialize our product candidates in the U.S., the EU and in additional foreign countries. While the scope of regulatory approval is similar in other countries, to obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing, and distribution of our product candidates, and we cannot predict success in these jurisdictions.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate CTA to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors could choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those are governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

Clinical trials are expensive, time-consuming, and difficult to design and implement, and involve an uncertain outcome.

Before obtaining marketing approval from the FDA, or other comparable foreign regulatory authorities, for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Although we are planning for certain clinical trials relating to BXCL501, BXCL701, BXCL502 and our other product candidates, there can be no assurance that the FDA, or other comparable foreign regulatory authorities, will accept our proposed trial designs. We may experience delays in our clinical trials, and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- the FDA, or comparable foreign regulatory authorities, disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory authorizations to commence a trial or consensus with regulatory authorities on trial designs;

- reaching agreement on acceptable terms with prospective contract research organizations ("CROs") and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- diversion of health care resources to combat epidemics, such as the COVID-19 pandemic;
- obtaining IRB approval at each site, or independent ethics committee approval at any sites outside the U.S.;
- dependence on the needs and timing of third-party collaborators;
- changes to clinical trial protocols;
- recruiting suitable patients to participate in a trial in a timely manner and in sufficient numbers;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing patient safety concerns that arise during the course of a trial;
- having patients complete a trial or return for post-treatment follow-up;
- imposition of a clinical hold by regulatory authorities, including as a result of unforeseen safety issues or side effects or failure of trial sites to adhere to regulatory requirements;
- the occurrence of SAEs in trials of the same class of agents conducted by other companies or institutions;
- subjects choosing an alternative treatment for the indications for which we are developing our product candidates, or participating in competing trials;
- adding a sufficient number of clinical trial sites;
- manufacturing sufficient quantities of a product candidate for use in clinical trials;
- lack of adequate funding to continue the clinical trial;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our product candidates, or any of their components, being ordered by the FDA, or comparable foreign regulatory authorities, to temporarily or permanently shut down due to violations of current cGMP regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule, or consistent with the clinical trial protocol, GCP or other regulatory requirements; or
- third-party contractors not performing data collection or analysis in a timely or accurate manner; or third-party contractors becoming debarred or suspended, or otherwise penalized by the FDA, or other government or regulatory authorities, for violations of regulatory requirements, in which case, we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting, or completing our planned and ongoing clinical trials. For

example, in April 2021, PLACIDITY enrollment was voluntarily paused to assess challenges posed in opening relevant clinical sites and enrolling delirium patients in ICU settings, and we also faced disruptions to our TRANQUILITY II trial, including as a result of the burden COVID-19.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board ("DSMB") for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, or other regulatory authorities, resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and, while we have agreements governing their committed activities, we have limited influence over their actual performance.

Further, conducting clinical trials in foreign countries, as we may do for our current and future product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol due to differences in health care services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. For example, if the current conflict between Russia and Ukraine spreads to other regions, it may adversely impact our ability to conduct trials.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition, and prospects significantly. 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.

We depend on enrollment of patients in our clinical trials to continue development of our product candidates. If we are unable to enroll patients in our clinical trials, our research and development efforts could be adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. Patient enrollment is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, the size of the patient population required for analysis of the trial's primary endpoints, our ability to recruit clinical trial investigators with the appropriate competencies and experience, our ability to obtain and maintain patient consents, the risk that patients enrolled in clinical trials will drop out of the trials before completion, and competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Our ability to enroll patients in our clinical trials has been, and may in the future be, impacted by governmental restrictions, and diversion of health care resources, resulting from the COVID-19 pandemic. Many pharmaceutical companies are conducting clinical trials in patients with the disease indications that our product candidates are designed to target. As a result, we must compete with them for clinical sites, physicians and the limited number of patients who fulfill the stringent requirements for participation in clinical trials. Also, due to the confidential nature of clinical trials, we do not know how many of the eligible patients may be enrolled in competing studies and who are consequently not available to us for our clinical trials. Our clinical trials may be delayed or terminated due to the inability to enroll enough patients. The delay or inability to meet planned patient enrollment may result in increased costs and delay or termination of our trials, which could have a harmful effect on our ability to develop products.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, or other comparable foreign authorities. The clinical evaluation of BXCL501, BXCL502, BXCL701, BXCL702 and our other product candidates in patients, in many cases, is ongoing and it is possible that there may be side effects associated with their use. Results of our trials could reveal a high and unacceptable severity and prevalence of these, or other, side effects. For example, in our Phase 2 clinical trial of BXCL701 for the treatment of emergent neuroendocrine prostate cancer, one patient experienced acidosis with a fatal outcome. Although the clinical investigator could not determine that the fatality was related to treatment with BXCL701, it is possible that BXCL701 could be tied to unacceptable side effects in the future.

If we observe drug-related AEs or other unacceptable safety concerns in clinical trials, we, the FDA, the IRBs at the institutions in which our studies are conducted, or the DSMB, could suspend or terminate our clinical trials, or the FDA, or comparable foreign regulatory authorities, could order us to cease clinical trials, or deny approval of our product candidates for any or all targeted indications. For example, the FDA placed Point Therapeutics, Inc.'s IND for BXCL701 on clinical hold following an increase in observed mortality in patients receiving BXCL701 in a Phase 3 trial in patients with non-small cell lung cancer. Though we believe that this result was caused by, among other things, an imbalance in the disease severity of patients enrolled in the active arm of the clinical trial, there is no guarantee that excess mortality will not be observed in future clinical studies. Treatment-related side effects could also affect patient recruitment, or the ability of enrolled patients to complete the clinical trial, or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles observed in our clinical trials and upon commercialization of any of our product candidates that may receive regulatory approval. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Additionally, if we or others later identify undesirable side effects caused by IGALMI, or any other product candidate that receives marketing approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such products;
- we may be required to recall a product or change the way such a product is administered to patients;
- additional restrictions may be imposed on the marketing or distribution of the particular product or the manufacturing processes for the product or any component thereof;
- regulatory authorities may require additional warnings on the label, such as a "black box" warning or contraindication;
- we may be required to implement REMS or create a medication guide outlining the risks of such side effects for distribution to patients, or similar risk management measures;
- we could be sued and held liable for harm caused to patients;
- our product may become less competitive; and
- our reputation may suffer.

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

BioXcel LLC's approach to the discovery and development of product candidates based on EvolverAI, its proprietary pharmaceutical discovery and development engine, is novel and unproven, and we do not know whether we will be able to develop any products of commercial value.

We are leveraging BioXcel LLC's EvolverAI, a proprietary pharmaceutical discovery and development engine, to create a pipeline of neuroscience and immuno-oncology product candidates for patients whose diseases have not been adequately addressed to date by other approaches and to design and conduct efficient clinical trials with a higher likelihood of success. While we believe that applying BioXcel LLC's EvolverAI to create medicines for defined patient populations may potentially enable drug research and clinical development that is more efficient than conventional drug research and development, our approach is novel. Although we obtained FDA approval for IGALMI, because our approach is novel, the cost and time needed to develop our product candidates is difficult to predict, and our efforts may not result in the discovery and development of commercially viable medicines. We may also be incorrect about the effects of our product and product candidates on the diseases of our defined patient populations, which may limit the utility of our approach or the perception of the utility of our approach. Furthermore, our estimates of our defined patient populations available for study and treatment may be lower than expected, which could adversely affect our ability to conduct clinical trials and may also adversely affect the size of any market for medicines we may successfully commercialize. Our approach may not result in time savings, higher success rates or reduced costs as we expect it to, and if not, we may not attract collaborators or develop new drugs as quickly or cost effectively as expected and therefore we may not be able to commercialize our approach as originally expected.

BioXcel LLC's EvolverAI may fail to help us discover and develop additional potential product candidates.

Any drug discovery that we are conducting using BioXcel LLC's EvolverAI may not be successful in identifying compounds that have commercial value or therapeutic utility. BioXcel LLC's EvolverAI may initially show promise in identifying potential product candidates, yet fail to yield viable additional product candidates for clinical development or potential commercialization for a number of reasons, including:

- research programs to identify new product candidates will require substantial technical, financial, and human resources, and we may be unsuccessful in our efforts to identify new product candidates. If we are unable to identify suitable additional compounds for preclinical and clinical development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price;
- compounds found through BioXcel LLC's EvolverAI may not demonstrate efficacy, safety or tolerability;
- potential product candidates may, on further study, be shown to have harmful side effects, or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance;
- competitors may develop alternative therapies that render our potential product candidates non-competitive or less attractive; or
- a potential product candidate may not be capable of being produced at an acceptable cost.

We obtained Fast Track designation for BXCL501 for the acute treatment of mild-to-moderate agitation associated with schizophrenia, bipolar disorder, and dementia, and we may seek Fast Track designation for other indications or for our other product candidates, but we might not receive such designations, and even if we do, such designations may not actually lead to a faster development or regulatory review or approval process.

If a product candidate is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a product sponsor may apply for FDA Fast Track designation. The sponsor of a Fast Track product candidate 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 if the relevant criteria are met. A Fast Track product candidate 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. We obtained Fast Track designation for BXCL501 for the acute treatment of mild-to-moderate agitation associated with schizophrenia, bipolar disorder, and dementia, and we may seek Fast Track designation for other indications or for one or more of our other product candidates, but we might not receive such designations from the FDA. However, even if we receive Fast Track designation, Fast Track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. In addition, 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.

A Breakthrough Therapy designation by the FDA, even if granted for any of our 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 marketing approval.

We obtained Breakthrough Therapy Designations for BXCL501 for the acute treatment of agitation associated with dementia, and we may seek additional Breakthrough Therapy designations for our product candidates if the clinical data support such a designation for one or more 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 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. Product candidates designated as Breakthrough Therapies by the FDA also receive the benefits associated with Fast Track designation, including the potential for rolling review of an NDA.

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 drugs considered for approval under non-expedited FDA review 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 the product no longer meets the conditions for qualification or decide that the period for FDA review or approval will not be shortened.

If the FDA does not conclude that our product candidates satisfy the requirements for the 505(b)(2) regulatory approval pathway, or if the requirements for approval of any of our product candidates under Section 505(b)(2) are not as we expect, the approval pathway for our product candidates will likely take significantly longer, cost significantly more, and encounter significantly greater complications and risks than anticipated, and in any case may not be successful.

We intend to seek FDA approval through the 505(b)(2) regulatory pathway for certain of our product candidates. The Hatch-Waxman Act added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies that were not conducted by or for the applicant. If the FDA does not allow us to pursue the 505(b)(2) regulatory pathway for our product candidates as anticipated, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for our product candidates would likely substantially increase. Moreover, the inability to pursue the 505(b)(2) regulatory pathway could result in new competitive products reaching the market faster than our product candidates, which could materially adversely impact our competitive position and prospects. Even if we are allowed to pursue the 505(b)(2) regulatory pathway for a product candidate, we cannot assure you that we will receive the requisite or timely approvals for commercialization of such product candidate. In addition, we expect that our competitors will file citizens' petitions with the FDA in an attempt to persuade the FDA that our product candidates, or the clinical studies that support their approval, contain deficiencies. Such actions by our competitors could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2).

If we are required by the FDA, or similar regulatory authorities, to obtain approval (or clearance, or certification) of a companion diagnostic device in connection with approval of one of our product candidates, and we do not obtain, or face delays in obtaining, approval (or clearance, or certification) of a companion diagnostic device, we will not be able to commercialize the product candidate, and our ability to generate revenue will be materially impaired.

According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. If a satisfactory companion diagnostic is not commercially available, we may be required to create or obtain one that would be subject to regulatory approval requirements. For example, we may decide to collaborate with patient diagnostic companies during our clinical trial enrollment process for BXCL701 to help identify patients with tumor gene alterations that we believe may be most likely to respond to treatment with BXCL701. The process of obtaining or creating such diagnostic is time consuming and costly.

Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices by the FDA and comparable foreign regulatory authorities, and, to date, the FDA has generally required premarket approval of companion diagnostics for cancer therapies. Generally, when a companion diagnostic is essential to the safe and effective use of a therapeutic product, the FDA requires that the companion diagnostic be approved before, or concurrent with, approval of the therapeutic product and before a product can be commercialized. The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect.

If the FDA, or a comparable foreign regulatory authority, requires approval (or certification or clearance) of a companion diagnostic for any of our product candidates, whether before or after the product candidate obtains marketing approval, we and/or third-party collaborators may encounter difficulties in developing and obtaining approval (or clearance, or certification) for these companion diagnostics. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval (or clearance, or certification) of a companion diagnostic could delay or prevent approval or continued marketing of our related product candidates. We may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our product candidates, if approved, on a timely or profitable basis, if at all.

Approval, clearance, or certification of companion diagnostics may be subject to further legislative or regulatory reforms, notably in the EU. On May 25, 2017, the new IVDR entered into force. The IVDR repeals and replaces the EU In Vitro Diagnostic Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the EU member states, regulations are directly applicable (i.e., without the need for adoption of EU member states laws implementing them) in all EU member states and are intended to eliminate current differences in the regulation of medical devices among EU member states. The IVDR, among other things, is intended to establish a uniform, transparent, predictable, and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. The IVDR became effective in May 2022. However, on October 14, 2021, the European Commission proposed a "progressive" roll-out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. The European Parliament and Council adopted the proposed regulation on December 15, 2021. The IVDR fully applied as of May 26, 2022, but there is a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation.

The regulation of companion diagnostics in the EU will be subject to further requirements since the IVDR introduces a new classification system for companion diagnostics. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authority or the EMA.

These modifications may make it more difficult and costly for us to obtain regulatory clearances, approvals, or certifications for our companion diagnostics or to manufacture, market or distribute our products after clearance, approval or certification is obtained.

Although the FDA has approved IGALMI for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder, we will still face extensive and ongoing regulatory requirements and obligations for IGALMI and for any product candidates for which we obtain approval.

Any regulatory approvals that we may receive for IGALMI or any of our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA-approved label for IGALMI includes certain warnings and precautions regarding hypotension, orthostatic hypotension, bradycardia, somnolence, and QT interval prolongation. The FDA may also require a REMS to approve a product candidate, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

In addition, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for IGALMI are and will remain subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, and on-going compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. If we or a regulatory authority discover previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

In addition, discovery of previously unknown AEs or other problems with our products, manufacturers or manufacturing processes or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of products;
- restrictions on product manufacturing, distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or

- injunctions or the imposition of civil or criminal penalties.

Further, the policies of the FDA and other regulatory authorities may change, and additional government regulations may be enacted that could impose extensive and ongoing regulatory requirements and obligations on any product candidate for which we obtain marketing approval. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad.

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

The FDA and other regulatory authorities strictly regulate marketing, labeling, advertising, and promotion of prescription drugs. These regulations include standards and restrictions for direct-to-consumer advertising, industry-sponsored scientific and educational activities, promotional activities involving the internet and off-label promotion. Any regulatory approval that the FDA or any other regulatory authority may grant is limited to those specific diseases. and indications for which a product is deemed to be safe and effective. For example, the FDA-approved label for IGALMI is currently limited to the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults.

While physicians in the U.S. may choose, and are generally permitted, to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote the products is narrowly limited to those indications that are specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. For example, other formulations of Dex, the active ingredient in IGALMI, have been approved for uses beyond those authorized in IGALMI approved labeling, such as for use in sedation of surgical patients, and we are continuing to develop BXCL501 for potential use in patients with dementia, MDD, Alzheimer's disease and other indications. We do not market or promote IGALMI for these uses.

Regulatory authorities in the U.S. generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies on off-label use. If we are found to have promoted our products for any off-label uses, the U.S. federal government (and other foreign governments) could levy civil, criminal and/or administrative penalties, and seek fines against us. The FDA, or other regulatory authorities, could also require that we enter into a consent decree or a corporate integrity agreement, or seek a permanent injunction against us, under which specified promotional conduct is monitored, changed or curtailed. If we cannot successfully manage the promotion of IGALMI or our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy 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, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result of some of these aforementioned issues. In addition, government funding of other government agencies 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, such as the EMA, following its relocation to Amsterdam and corresponding staff changes, may also slow the time necessary for new drug or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of

domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the U.S. have adopted similar restrictions or other policy measures in response to the 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 or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We may conduct certain of or portions of our clinical trials for our product candidates outside of the U.S. and the FDA may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

We may choose to conduct one or more of our clinical trials, or a portion of our clinical trials, for our product candidates outside the U.S. The acceptance of study data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, if the clinical trial was not otherwise subject to an IND, the FDA will not accept the data as support for an application for marketing approval unless the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data from the study through an on-site inspection, if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and could result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

We may be subject to extensive regulations outside the U.S. and may not obtain marketing approvals for products in Europe and other jurisdictions.

In addition to regulations in the U.S., should we or our collaborators pursue marketing approvals for IGALMI, and for BXCL501, BXCL502, BXCL701, BXCL702 and our other product candidates internationally, we and our collaborators will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we, or our collaborators, obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country.

We expect to pursue marketing approvals for IGALMI, and may pursue marketing approvals for BXCL501, BXCL502, BXCL701, BXCL702 and our other product candidates in Europe and other jurisdictions outside the U.S. with collaborative partners. The time and process required to obtain regulatory approvals and reimbursement in Europe and other jurisdictions may be different from those in the U.S. Also, regulatory approval in one jurisdiction does not ensure approvals in any other jurisdiction; however, negative regulatory decisions in any jurisdiction may have a negative impact on the regulatory process in other jurisdictions.

Following a national referendum and enactment of legislation by the government of the UK, the UK formally withdrew from the EU on January 31, 2020, and ratified a trade and cooperation agreement governing its future relationship (commonly referred to as “Brexit”). The agreement, which was applied provisionally from January 1, 2021 and entered into force on May 1, 2021, addresses trade, economic arrangements, law enforcement, judicial cooperation

and a governance framework including procedures for dispute resolution, among other things. Because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the UK and the EU as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

Since January 1, 2021, the UK operates under a distinct regulatory regime to the EU. EU pharmaceutical laws only apply in respect of the UK to Northern Ireland (as set out in the Protocol on Ireland/Northern Ireland). EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". While the UK has indicated a general intention that new laws regarding the development, manufacture, and commercialization of medicinal products in the UK will align closely with EU law, there are limited detailed proposals for future regulation of medicinal products. The trade and cooperation agreement includes specific provisions concerning medicinal products, which include the mutual recognition of cGMP, inspections of manufacturing facilities for medicinal products and cGMP documents issued (such mutual recognition can be rejected by either party in certain circumstances) but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. For example, it is not clear to what extent the UK will adopt legislation aligned with, or similar to, the EU CTR which became applicable on January 31, 2022, and which significantly reforms the assessment and supervision processes for clinical trials throughout the EU. On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency ("MHRA") launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022, and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation will be closely watched and will determine whether the UK chooses to align with the regulation or diverge from it to maintain regulatory flexibility. A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK.

Therefore, there remains political and economic uncertainty regarding to what extent the regulation of medicinal products will differ between the UK and the EU in the future. Any divergences will increase the cost and complexity of running our business, including with respect to the conduct of clinical trials. Brexit also materially impacted the regulatory regime with respect to the approval of our product candidates. Great Britain is no longer covered by the EU's procedures for the grant of MAs (Northern Ireland is covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). As of January 1, 2021, all existing Centralized MAs were automatically converted into UK MAs effective in Great Britain and issued with a UK MA number on January 1, 2021 (unless MA holders opted out of this scheme). A separate MA is now required to market drugs in Great Britain. It is currently unclear whether the regulator in the UK, the MHRA, is sufficiently prepared to handle the increased volume of MAAs that it is likely to receive. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in Great Britain and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in Great Britain for our product candidates, which could significantly and materially harm our business. The UK's withdrawal from the EU and the associated uncertainty has had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Any of these factors could have a significant adverse effect on our business, financial condition, results of operations and prospects.

Further, the UK's withdrawal from the EU has resulted in the relocation of the EMA from the UK to the Netherlands. This relocation has caused, and may continue to cause, disruption in the administrative and medical scientific links between the EMA and the MHRA, including delays in granting clinical trial authorization or MA, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to MA and commercialization of products in the EU and/or the UK.

If we are found in violation of federal, state or foreign health care "fraud and abuse" laws, we may be required to pay significant fines and penalties, including, without limitation, debarment, suspension or exclusion from participation in federal, state or similar health care programs, which may adversely affect our business, financial condition and results of operations.

In the U.S., we are subject to various federal and state health care "fraud and abuse" laws, including anti- kickback laws, false claims laws and other laws intended to reduce fraud and abuse in federal and state health care programs, which could affect us, and our ability to successfully commercialize our products in the U.S. We may have to comply with similar laws and regulations outside the U.S. These laws include:

- the federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce the referral of business, including the purchase, order or prescription of a particular drug for which payment may be made under a federal health care program, such as Medicare or Medicaid. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it to have committed a violation;

- false claims laws prohibit anyone from knowingly and willfully presenting or causing to be presented for payment to third-party payers, including government payers, claims for reimbursed drugs or services that are false or fraudulent, claims for items or services that were not provided as claimed, or claims for medically unnecessary items or services. Cases have been brought under false claims laws alleging that off-label promotion of pharmaceutical products or the provision of kickbacks has resulted in the submission of false claims to governmental health care programs. 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 false claims laws. Further, private individuals have the ability to bring actions on behalf of the government under the federal False Claims Act;

- HIPAA prohibits persons or entities from knowingly and willfully executing a scheme to defraud any health care benefit program, including private payers, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation;

- federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state health care program beneficiary if the person knows, or should know, it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- the Sunshine Act, as amended by the ACA, which requires certain manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Centers for Medicare & Medicaid Services ("CMS") information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants, and certified nurse midwives), and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members;

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to 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 applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to health care providers and other potential referral sources; and state laws that

require drug manufacturers to report information related to payments and other transfers of value to physicians and other health care providers or marketing expenditures and pricing information; and

- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to health care providers.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state or foreign health care programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to market our products and adversely impact our financial results.

We may be unable to maintain sufficient clinical trial liability insurance.

Our inability to retain sufficient clinical trial liability insurance at an acceptable cost to protect against potential liability claims could prevent or inhibit our ability to conduct clinical trials for product candidates we develop. We may be unable to obtain appropriate levels of such insurance. Even if we do secure clinical trial liability insurance for our programs, we may not be able to achieve sufficient levels of such insurance. Any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that exceeds the limits of our insurance coverage. We have supplemented our clinical trial coverage with product liability coverage in connection with the commercial launch of IGALMI, and expect that we would similarly supplement our coverage for any of our other product candidates that may receive regulatory approval, but we may be unable to obtain such increased coverage on acceptable terms or at all. If we are found liable in a clinical trial lawsuit or a product liability lawsuit in the future, we will 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.

Risks Related to Commercialization of Our Product Candidates

If our products do not gain market acceptance, our business will suffer because we might not be able to fund future operations.

A number of factors may affect the market acceptance of our products or any other products or product candidates we develop or acquire, including, among others:

- the price of our products relative to other products for the same or similar treatments;
- the perception by patients, physicians and other members of the health care community of the effectiveness, utility and safety of our products for their indicated applications and treatments;
- our ability to fund our sales and marketing efforts; and
- the effectiveness of our sales and marketing efforts.

If our products do not gain market acceptance, we may not be able to fund future operations, including developing, testing and obtaining regulatory approval for new product candidates and expanding our sales and marketing efforts for our approved products, which would cause our business to suffer.

We obtained Orphan Drug Designation for BXCL701 for the treatment of pancreatic cancer, melanoma, acute myeloid leukemia and soft tissue sarcoma and we may seek Orphan Drug Designation for other indications or product candidates, and we may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity, and may not receive Orphan Drug Designation for other indications or for our other product candidates.

Regulatory authorities in some jurisdictions, including the U.S. and EU, may designate drugs intended for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug 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 in the U.S., or a patient population greater than 200,000 individuals in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the EU, orphan drug designation is granted by the European Commission based on a scientific opinion of the EMA's Committee for Orphan Medicinal Products. A medicinal product may be designated as orphan if its sponsor can establish that (i) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (ii) either (a) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the medicinal product will be of significant benefit to those affected by the condition. The application for orphan designation must be submitted before the MAA.

In the U.S., orphan drug designation 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 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 drug exclusivity. Orphan drug exclusivity in the U.S. provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same disease or condition for seven years. In limited circumstances, the applicable exclusivity period is 10 years in the EU. The EU exclusivity period can be reduced to six years if, at the end of the fifth year, it is established that a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

In January 2021, the FDA granted Orphan Drug Designation to BXCL701 for the treatment of soft tissue sarcoma. In September 2019, the FDA granted Orphan Drug Designation to BXCL701 for the treatment of acute myeloid leukemia. Prior to 2019, the FDA granted Orphan Drug Designation to BXCL701 for the treatment of pancreatic cancer and melanoma. We may seek Orphan Drug Designations for BXCL701 in other diseases or conditions or for other product candidates. There can be no assurances that we will be able to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, 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 orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products, and it is possible that another company also holding orphan drug designation for the same product candidate will receive marketing approval for the same disease or condition before we do. If that were to happen, our applications for that disease or condition may not be approved until the competing company's period of exclusivity expires. In addition, exclusive marketing rights in the U.S. and abroad may be limited if we seek approval for an indication broader than the orphan-designated disease or condition or may be lost if the FDA or foreign regulatory authorities later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active ingredients may be approved for the same disease or condition. Even after an orphan drug is approved, the FDA or foreign regulatory authorities can subsequently approve the same drug with the same active ingredient for the same condition if the FDA or foreign regulatory authorities conclude 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 or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process and does not prevent competitors from obtaining approval of the same product candidate as ours for indications other than those in which we have been granted orphan drug designation.

If we are unable to develop satisfactory sales and marketing capabilities, we may not succeed in commercializing IGALMI or any product candidate for which we may obtain regulatory approval.

We have limited experience in marketing and selling drug products. We have not entered into arrangements for the sale and marketing of IGALMI or BXCL501, BXCL502, BXCL701, BXCL702 or any other product candidate. Typically, pharmaceutical companies would employ groups of sales representatives and associated sales and marketing staff numbering in the hundreds to thousands of individuals to call on the large number of physicians and hospitals. We may seek to collaborate with a third-party to market our drugs or may seek to market and sell our drugs by ourselves. If we seek to collaborate with a third-party, we cannot be sure that a collaborative agreement can be reached on terms acceptable to us. We may also need to hire additional personnel skilled in marketing and sales for our direct marketing and selling efforts. We cannot be sure that we will be able to acquire, or establish third-party relationships to provide, any or all of these marketing and sales capabilities. The maintenance and expansion of our direct sales force or establishment of a contract sales force, or a combination thereof, as applicable, to market our products is expensive and time-consuming and could delay any product launch. Further, we can give no assurances that we will be able to maintain a direct and/or contract sales force for any period of time or that our sales efforts will be sufficient to grow our revenues or that our sales efforts will ever lead to profits.

We operate in a highly competitive and rapidly changing industry.

Biopharmaceutical product development is highly competitive and subject to rapid and significant technological advancements. Our success is highly dependent upon our ability to in-license, acquire, develop and obtain regulatory approval for new and innovative products on a cost-effective basis and to market them successfully. In doing so, we face and will continue to face intense competition from a variety of businesses, including large, fully integrated, well-established pharmaceutical companies who already possess a large share of the market, specialty pharmaceutical and biopharmaceutical companies, academic institutions, government agencies and other private and public research institutions in the U.S., the EU and other jurisdictions.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved drugs than we do. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the biopharmaceutical industry could result in even more resources being concentrated among a small number of our competitors.

Competition may further increase as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop.

Established biopharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability, and safety to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing, receiving FDA approval for or commercializing drugs before we do, which would have an adverse impact on our business and results of operations.

The availability of our competitors' products could limit the demand and the price we are able to charge for products and product candidates, if any, that we commercialize. The inability to compete with existing or subsequently introduced drugs would harm our business, financial condition, and results of operations.

Although we obtained FDA approval for IGALMI, our products and product candidates may not be accepted by physicians or the medical community in general.

There can be no assurance that IGALMI, or BXCL501, BXCL502, BXCL701, BXCL702 and our other product candidates or any other product candidate successfully developed by us, independently or with partners, if approved, will be accepted by physicians, hospitals, and other health care facilities. IGALMI competes, and BXCL501, BXCL502, BXCL701, BXCL702 and any future product candidates we develop will compete, with a number of products manufactured and marketed by major pharmaceutical and biotechnology companies. The degree of market acceptance of IGALMI and any drugs we develop depends on a number of factors, including:

- our demonstration of the clinical efficacy and safety of our products and product candidates;
- timing of market approval and commercial launch of our products and product candidates;
- the clinical indication(s) for which our products and product candidates are approved;
- product label and package insert requirements;
- advantages and disadvantages of our products and product candidates compared to existing therapies;
- continued interest in and growth of the market for anti-cancer or anti-agitation drugs;
- strength of sales, marketing, and distribution support;
- product pricing in absolute terms and relative to alternative treatments;
- future changes in health care laws, regulations, and medical policies; and
- availability of coverage and reimbursement in select jurisdictions, and future changes to coverage and reimbursement policies of government and third-party payors.

Significant uncertainty exists as to the coverage and reimbursement status of IGALMI or any product candidate for which we obtain regulatory approval. In the U.S. and other countries, sales of IGALMI and any other products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations.

Third-party payors are increasingly challenging the prices charged for medical products and services. It will be time consuming and expensive for us to go through the process of seeking coverage and reimbursement from Medicare and private payors. IGALMI and any other products for which we receive regulatory approval may not be considered cost-effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our proposed products on a profitable basis. Further federal, state and foreign government proposals and health care reforms are likely which could limit the prices that can be charged for IGALMI and the product candidates that we develop and may further limit our commercial opportunities. Our results of operations could be materially adversely affected by proposed health care reforms, by the Medicare prescription drug coverage legislation in the U.S., by the possible effect of such current or future legislation on amounts that private insurers will pay and by other health care reforms that may be enacted or adopted in the future.

Health care reform measures could hinder or prevent our product candidates' commercial success.

The U.S. government and other governments have shown significant interest in pursuing health care reform. Any government-adopted reform measures could adversely impact the pricing of health care products and services in the U.S. or internationally and the amount of reimbursement available from governmental agencies or other third-party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce health care costs may adversely affect our ability to set prices for our products, which we believe are fair, and our ability to generate revenues and achieve and maintain profitability.

New laws, regulations and judicial decisions, or new interpretations of existing laws, regulations and decisions, that relate to health care availability, methods of delivery or payment for products and services, or sales, marketing or pricing, may limit our potential revenue, and we may need to revise our research and development programs. The pricing and reimbursement environment may change in the future and become more challenging due to several reasons, including policies advanced by the current executive administration in the U.S., new health care legislation or fiscal challenges faced by government health administration authorities. Specifically, in both the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the health care system in ways that could affect our ability to sell our products profitably.

For example, in the U.S., the ACA has substantially changed the way health care is financed by both government health plans and private insurers, and significantly impacts the pharmaceutical industry. For example, the ACA imposed a non-deductible excise tax on pharmaceutical manufacturers or importers that sell branded prescription drugs to government programs. In addition, as part of the ACA's provisions closing a funding gap that existed in the Medicare Part D prescription drug program, manufacturers are required to provide a discount on branded prescription drugs for drugs provided to certain beneficiaries who fall within the "donut hole." Similarly, the ACA increased the level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1% of the average manufacturer price and required collection of rebates for drugs paid by Medicaid managed care organizations. The ACA also included changes to the Public Health Service's 340B drug pricing program (the "340B program") including expansion of the list of eligible covered entities that may purchase drugs under the program.

Since its enactment, there have been judicial, executive 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. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15,2021 through August 15, 2021. The executive order instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to health care, 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.

In addition, other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. These changes include the Budget Control Act of 2011, which resulted in aggregate reductions of Medicare payments to providers, which went into effect on April 1, 2013, and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, unless additional Congressional action is taken. Furthermore, the American Taxpayer Relief Act of 2012, further reduced Medicare payments to several types of providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Most significantly, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 ("IRA") into law. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated, and while the impact of the IRA on the pharmaceutical industry and our business cannot yet be fully determined, it is likely to be significant.

The cost of prescription pharmaceuticals in the U.S. will likely continue to be the subject of considerable discussion. Members of Congress and the Biden Administration have indicated they will continue to pursue further legislative or administrative measures to control prescription drug costs. There have been several Congressional inquiries, as well as legislative and regulatory initiatives and executive orders designed to, among other things, bring more transparency to

product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. We cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

Individual states in the U.S. continue to consider and have enacted legislation to limit the growth of health care costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information. If we are found to have violated state law requirements, we may become subject to penalties or other enforcement mechanisms, which could have a material adverse effect on our business. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

It is likely that federal and state legislatures within the U.S. and foreign governments will continue to consider changes to existing health care legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce costs of health care may adversely affect the demand for IGALMI and any other drug products for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain adequate coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

In the EU, similar developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the U.S. and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment (“HTA”) amending Directive 2011/24/EU, was adopted. While the regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be

responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

If we fail to comply with reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the U.S., we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, results of operations and financial condition.

We participate in the Medicaid Drug Rebate Program ("MDRP") and other federal and state government pricing programs in the U.S., and we may participate in additional government pricing programs in the future. These programs generally require manufacturers to pay rebates or otherwise provide discounts to government payors in connection with drugs that are dispensed to beneficiaries of these programs. As a condition of having federal funds being made available for covered outpatient drugs under Medicaid and Medicare Part B, a manufacturer must enroll in the MDRP. Under this program, we must pay a rebate to state Medicaid programs for each unit of our covered outpatient drug dispensed to a Medicaid beneficiary and paid for by a state Medicaid program. Medicaid drug rebates are based on pricing data that we must report on a monthly and quarterly basis to CMS. For the MDRP, this data includes the average manufacturer price ("AMP") for each drug and, in the case of an innovator product, like IGALMI, the best price. If we become aware that our MDRP price reporting submission for a prior period was incorrect or has changed, as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after the data originally was due. Further, under the IRA, AMP figures we report will also be used to calculate a rebate on Medicare Part D utilization, triggered by price increases that outpace inflation. If we fail to provide information timely or are found to have knowingly submitted false information to the government, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP, which would result in payment not being available for our covered outpatient drugs under Medicaid or, if applicable, Medicare Part B. Failure to make necessary disclosures and/or to identify overpayments additionally could result in allegations against us under the Federal False Claims Act and other laws and regulations.

Federal law requires that a manufacturer that participates in the MDRP also participate in the 340B program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B, and we participate in the 340B program. The 340B program is administered by the Health Resources and Services Administration ("HRSA") and requires us to charge statutorily defined covered entities no more than the 340B program "ceiling price" for its covered outpatient drugs used in an outpatient setting. These 340B program covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B program ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B program ceiling price calculation and discount requirement. We must report 340B program ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B program covered entities. HRSA has finalized regulations regarding the calculation of the 340B program ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B program eligible drugs. HRSA has also finalized an administrative dispute resolution process through which 340B program covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B program covered entities for engaging in unlawful diversion or duplicate discounting of 340B program drugs. In addition, legislation may be introduced that, if passed, would further expand the 340B program, such as adding further covered entities or requiring participating manufacturers to agree to provide 340B program discounted pricing on drugs used in an inpatient setting.

In order to be eligible to have drug products paid for with federal funds under Medicaid and Medicare Part B and purchased by certain federal agencies and grantees, we also must participate in the U.S. Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program. Under the VA/FSS program, we must report the Non-Federal Average Manufacturer Price ("Non-FAMP") for our covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non-FAMP using a statutory formula. These four agencies are the VA, the U.S. Department of Defense, the U.S. Coast Guard, and the U.S. Public Health Service (including the Indian Health Service). We must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. If we fail to provide timely information or are found to have knowingly submitted false information, we may be subject to civil monetary penalties.

Individual states continue to consider and have enacted legislation to limit the growth of health care costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information. If we are found to have violated state law requirements, we may become subject to penalties or other enforcement mechanisms, which could have a material adverse effect on our business.

Pricing and rebate calculations are complex, vary among products and programs, and are often subject to interpretation by manufacturers, governmental or regulatory agencies, and the courts. The terms, scope and complexity of these government pricing programs change frequently, as do interpretations of applicable requirements for pricing and rebate calculations. Responding to current and future changes may increase our costs and the complexity of compliance will be time consuming. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. Price recalculations under the MDRP also may affect the ceiling price at which we may be required to offer products under the 340B program. Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we fail to submit required price data on a timely basis, or if we are found to have charged 340B program covered entities more than the statutorily mandated ceiling price. In the event that CMS were to terminate our Medicaid rebate agreement, pursuant to which we participate in the MDRP, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs. We cannot assure you that price data submissions we make will not be found to be incomplete or incorrect.

Risks Related to Our Relationship with BioXcel LLC

BioXcel LLC has significant influence over the direction of our business, and the concentrated ownership of our common stock will prevent you and other stockholders from influencing significant decisions.

As of December 31, 2022, BioXcel LLC owned approximately 30% of the economic interest and voting power of our outstanding common stock. Drs. Vimal Mehta and Krishnan Nandabalan are the co-founders and serve as senior executives and members of the board of BioXcel LLC. See “The management of and beneficial ownership in BioXcel LLC by our executive officers and our directors may create, or may create the appearance of, conflicts of interest.” below. Even though BioXcel LLC controls less than a majority of the voting power of our outstanding common stock, it may influence the outcome of such corporate actions so long as it owns a significant portion of our common stock.

Approval of commercial terms between us and BioXcel LLC does not preclude the possibility of stockholder litigation, including but not limited to derivative litigation nominally against BioXcel LLC and against its directors and officers and also against us and our directors and officers.

The commercial terms of the Services Agreement and the Contribution Agreement that we entered into with BioXcel LLC have not been negotiated by persons consisting solely of disinterested directors.

No assurance can be given that any stockholder of BioXcel LLC or the Company will not claim in a lawsuit that such terms in fact are not in the best interests of BioXcel LLC or the Company and its applicable equity holders, that the directors and officers of BioXcel LLC or the Company breached their fiduciary duties in connection with such agreements and that any disclosures by the Company to its stockholders regarding these agreements and the relationship between BioXcel LLC and us did not satisfy applicable requirements. In any such instance, we and our directors and officers may also be named as defendants, and we would have to defend ourselves and our directors and officers. While we would seek indemnification from BioXcel LLC under the terms of these agreements against any damages or other costs which could be substantial, no such indemnification has yet been agreed to or may be agreed to and be in effect. Further, any such litigation would be time-consuming and would divert focus and resources from the development of our

product candidates and our business, including but not limited to possibly delaying our clinical trials due to our management having to spend time and attention on such litigation.

We continue to depend on BioXcel LLC to provide us with certain services for our business.

We rely, in part, on BioXcel LLC and access to its EvolverAI, a research and development engine created and owned by BioXcel LLC, to identify, research and develop potential product candidates in neuroscience and immuno-oncology. We negotiated the Services Agreement with BioXcel LLC pursuant to which BioXcel LLC shall perform product identification and related services for us utilizing its EvolverAI. Under the Services Agreement, we have an option, exercisable until December 31, 2024, to enter into a collaborative services agreement with BioXcel LLC pursuant to which BioXcel LLC shall perform product identification and related services for us utilizing its EvolverAI. To maintain the ability to exercise the foregoing option, pursuant to an amendment to the Services Agreement effective as of April 19, 2022, the Company has agreed to pay BioXcel LLC $18,000 per month from March 13, 2023, to December 31, 2024. The parties are obligated to negotiate the collaborative services agreement in good faith and to incorporate reasonable market-based terms, including consideration for BioXcel LLC reflecting a low, single-digit royalty on net sales and reasonable development and commercialization milestone payments, provided that (i) development milestone payments shall not exceed $10 million in the aggregate and not be payable prior to proof of concept in humans and (ii) commercialization milestone payments shall be based on reaching annual net sales levels, be limited to 3% of the applicable net sales level, and not exceed $30 million in the aggregate. BioXcel LLC shall continue to make such product identification and related services available to us until at least December 31, 2024.

In addition, at the time of the our initial public offering (“IPO”), BioXcel LLC granted us (i) a first right to negotiate exclusive rights to any additional product candidates in the fields of neuroscience and immuno-oncology that BioXcel LLC may identify on its own and not in connection with BioXcel LLC’s provision of services to us under the Services Agreement and (ii) an exclusivity agreement in the neuroscience and immuno-oncology fields whereby BioXcel LLC agreed not develop drugs, or engage in preclinical discovery for the purpose of developing drugs, in the neuroscience and immuno-oncology fields for or on behalf of a third party, utilizing EvolverAI or otherwise. This first right to negotiate and exclusivity period expired on March 12, 2023 and there is no assurance that we will extend the terms of the agreement. We are assessing our ongoing business needs. If our rights under the Services Agreement were to become limited, or if we are otherwise precluded from conducting research and development using EvolverAI, or if BioXcel LLC is unable to fulfill its obligations under the agreements, such development could materially adversely affect our future operating results, financial condition, and prospects. Furthermore, certain individuals conducting services on our behalf are not our employees, and we cannot control whether they devote sufficient time, skill, and resources to our ongoing development programs. We also cannot ensure that BioXcel LLC retains sufficient resources or personnel or otherwise to conduct its operations. BioXcel LLC may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting research and development activities, which could impede their ability to devote appropriate time to our research and development programs. If we do not extend the exclusivity period in the neuroscience and immuno-oncology fields, BioXcel LLC will not be restricted from using EvolverAI to perform drug discovery services for our direct competitors, which could harm our competitive position and adversely affect our future operating results and financial condition.

The management of and beneficial ownership in BioXcel LLC by our executive officers and our directors may create, or may create the appearance of, conflicts of interest.

The management of and beneficial ownership in BioXcel LLC by our executive officers and our directors may create, or may create the appearance of, conflicts of interest. For example, our Chief Executive Officer and a director on our Board, Vimal Mehta, Ph.D., and our Chief Digital Officer and a director on our Board, Krishnan Nandabalan, Ph.D., are managers of BioXcel LLC, as well as directors, officers and stockholders of BioXcel LLC, BTI’s former parent company. Additionally, as of December 31, 2022, Dr. Mehta and Dr. Nandabalan, through their beneficial ownership of BioXcel LLC, owned approximately 33% and 31%, respectively of the Company. Management and ownership by our executive officers and directors in BioXcel LLC, creates, or may create the appearance of, conflicts of interest when these individuals are faced with decisions that could have different implications for BioXcel LLC than the decisions have for us, including decisions that relate to our Services Agreement and Contribution Agreement, as well as potential agreements relating to future product candidates and AI-related services or collaborations. Any perceived conflicts of

interest resulting from investors questioning the independence of our management or the integrity of corporate governance procedures may materially affect our stock price.

Any disputes that arise between us and BioXcel LLC with respect to our past and ongoing relationships could harm our business operations.

Disputes may arise between BioXcel LLC and us in a number of areas relating to our past and ongoing relationships, including:

- intellectual property, technology and business matters, including failure to make required technology transfers and failure to comply with non-compete provisions applicable to BioXcel LLC and us;
- labor, tax, employee benefit, indemnification and other matters arising from the separation of BTI from BioXcel LLC;
- distribution and supply obligations;
- employee retention and recruiting;
- business combinations involving us;
- sales or distributions by BioXcel LLC of all or any portion of its ownership interest in us;
- the nature, quality and pricing of services BioXcel LLC has agreed to provide us; and
- business opportunities that may be attractive to both BioXcel LLC and us.

We entered into the Services Agreement with BioXcel LLC related to the separation of our business operations from those of BioXcel LLC that contains certain limitations on BioXcel LLC's ability to control various aspects of our business and operations, notwithstanding BioXcel LLC's substantial ownership position. This agreement may be amended upon agreement between us and BioXcel LLC**.**

BioXcel LLC may experience challenges with the acquisition, development, enhancement or deployment of technology necessary for EvolverAI.

BioXcel LLC operates in businesses that require sophisticated computer systems and software for data collection, data processing, cloud-based platforms, analytics, statistical projections and forecasting, mobile computing, social media analytics and other applications and technologies. BioXcel LLC seeks to address its technology risks by increasing its reliance on the use of innovations by cross-industry technology leaders and adapt these for their pharmaceutical, biotechnology, biopharmaceutical, diagnostic, medical device and contract research and manufacturing clients. Some of the technologies supporting the industries they serve are changing rapidly and we must continue to adapt to these changes in a timely and effective manner at an acceptable cost. They also must continue to deliver data to their clients in forms that are easy to use while simultaneously providing clear answers to complex questions. There can be no guarantee that we or BioXcel LLC will be able to develop, acquire or integrate new technologies, that these new technologies will meet our and BioXcel LLC's needs or achieve our expected goals, or that we will be able to do so as quickly or cost-effectively as our competitors. Significant technological change could render BioXcel LLC's EvolverAI obsolete. BioXcel LLC's continued success will depend on its ability to adapt to changing technologies, manage and process ever-increasing amounts of data and information and improve the performance, features, and reliability of its services in response to changing client and industry demands. BioXcel LLC may experience difficulties that could delay or prevent the successful design, development, testing, and introduction of advanced versions of EvolverAI, limiting our ability to identify new product candidates. New services, or enhancements to existing EvolverAI services, may not adequately meet our requirements. Any of these failures could have a material adverse effect on our operating results and financial condition.

Risks Related to Our Reliance on Third Parties

We are substantially dependent on third parties for the manufacture of our clinical supplies of our product candidates and our commercial supplies of IGALMI, and we intend to rely on third parties to produce commercial supplies of any other approved product candidate. Therefore, our development of our products could be stopped or delayed, and our commercialization of any future product could be stopped or delayed or made less profitable if third-party manufacturers fail to obtain approval of the FDA or comparable regulatory authorities or fail to provide us with drug product in sufficient quantities or at acceptable prices.

We entered into a commercial supply agreement with ARx, LLC ("ARx") pursuant to which ARx has agreed to exclusively manufacture and supply us with all of our worldwide demand of film formulation of Dex to be used for the commercial supply of IGALMI and for ongoing clinical trials of our product candidate BXCL501, subject to certain alternative supply provisions. If ARx is unable to produce our supply of Dex, our business would be harmed because there can be no assurance that we will be able to identify or enter into agreements with alternative suppliers on a timely basis on acceptable terms, if at all. An interruption in our ability to sell our products to customers could occur if we encounter delays or difficulties in securing Dex, or if the quantity or quality supplied does not meet our specifications, or if we cannot then obtain an acceptable substitute. If any of these events occur, our business and operating results could be harmed. Our specified minimum annual payment could adversely affect our cash flows, such as in times when we have sufficient inventory and would otherwise be able to use our cash for other purposes.

The manufacture of biotechnology and pharmaceutical products is complex and requires significant expertise, capital investment, process controls and know-how. Common difficulties in biotechnology and pharmaceutical manufacturing may include sourcing and producing raw materials, transferring technology from chemistry and development activities to production activities, validating initial production designs, scaling manufacturing techniques, improving costs and yields, establishing and maintaining quality controls and stability requirements, eliminating contaminations and operator errors, and maintaining compliance with regulatory requirements. We do not currently have nor do we plan to acquire the infrastructure or capability internally to produce an adequate supply of compounds to meet future requirements for clinical trials and commercialization of our products or to produce our products in accordance with cGMP prescribed by the FDA or similar foreign requirements. Drug manufacturing facilities are subject to inspection before the FDA or foreign regulatory authorities will issue an approval to market a new drug product, and ARx, the Patheon pharma services division of Thermo Fisher Scientific Inc., and any other manufacturers that we may use must adhere to the cGMP or similar foreign regulations prescribed by the FDA or foreign regulatory authorities.

As such, these third-party manufacturers will be required to comply with cGMPs, and other applicable laws and regulations. We have no control over the ability of these third parties to comply with these requirements, or to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authorities do not approve the facilities of these third parties for the manufacture of our other product candidates or any products that we may successfully develop, or if it withdraws any such approval, or if our suppliers or contract manufacturers decide they no longer want to supply or manufacture for us, we may need to find alternative manufacturing facilities, in which case we might not be able to identify manufacturers for clinical or commercial supply on acceptable terms, or at all. Any of these factors would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates and adversely affect our business.

We, ARx, the Patheon pharma services division of Thermo Fisher Scientific Inc., and/or our other third-party manufacturers may be adversely affected by developments outside of our control, and these developments may delay or prevent further manufacturing of our products. Adverse developments may include labor disputes, resource constraints, shipment delays, inventory shortages, lot failures, unexpected sources of contamination, lawsuits related to our manufacturing techniques, equipment used during manufacturing, or composition of matter, unstable political environments, acts of terrorism, war, natural disasters, and other natural and man-made disasters. If BioXcel LLC, we, ARx, the Patheon pharma services division of Thermo Fisher Scientific Inc., or our other third-party manufacturers were to encounter any of the above difficulties, or otherwise fail to comply with contractual obligations, our ability to provide any product for clinical trial or commercial purposes would be jeopardized. This may increase the costs associated with completing our clinical trials and commercial production. Further, production disruptions may cause us to terminate ongoing clinical trials and/or commence new clinical trials at additional expense. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications or pass safety inspections.

Moreover, as a result of the COVID-19 pandemic, third-party manufacturers have been and may in the future be affected, which could disrupt their activities and, as a result, we could face difficulty sourcing key components necessary to produce supply of our commercial product and product candidates, which may negatively affect our preclinical and clinical development activities. If production difficulties cannot be solved with acceptable costs, expenses, and timeframes, we may be forced to abandon our clinical development and commercialization plans, which could have a material adverse effect on our business, prospects, financial condition, and the value of our securities.

We, or third-party manufacturers on whom we rely, including ARx, may be unable to successfully scale-up manufacturing of our product and product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing any approved products.

In order to conduct clinical trials of our product candidates and commercialize any approved product candidates, we, or our manufacturers, including ARx and the Patheon pharma services division of Thermo Fisher Scientific Inc., will need to manufacture them in large quantities. We, or our manufacturers, may be unable to successfully increase the manufacturing capacity for any of our approved products or product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any of our manufacturers, are unable to successfully scale up the manufacture of our approved products or product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. If we are unable to obtain or maintain third-party manufacturing for commercial supply of our approved products, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our approved products or product candidates successfully.

Our failure to find third-party collaborators to assist or share in the costs of product development could materially harm our business, financial condition, and results of operations.

Our strategy for the development and commercialization of our proprietary products and product candidates may include the formation of collaborative arrangements with third parties. Collaborators have significant discretion in determining the efforts and resources they apply and may not perform their obligations as expected. Potential third-party collaborators include biopharmaceutical, pharmaceutical and biotechnology companies, academic institutions and other entities. Third-party collaborators may assist us in:

- funding research, preclinical development, clinical trials and manufacturing;
- seeking and obtaining regulatory approvals; and
- successfully commercializing IGALMI or product candidates.

If we are not able to establish collaboration agreements, we may be required to undertake product development and commercialization at our own expense. Such an undertaking may limit the number of product candidates that we will be able to develop, significantly increase our capital requirements and place additional strain on our internal resources. Our failure to enter into collaborations could materially harm our business, financial condition and results of operations.

In addition, our dependence on licensing, collaboration, and other agreements with third parties may subject us to a number of risks. These agreements may not be on terms that prove favorable to us and may require us to relinquish certain rights in our product candidates. To the extent we agree to work exclusively with one collaborator in a given area, our opportunities to collaborate with other entities could be curtailed. Lengthy negotiations with potential new collaborators may lead to delays in the research, development, or commercialization of product candidates. The decision by our collaborators to pursue alternative technologies, or the failure of our collaborators to develop or commercialize successfully any product candidate to which they have obtained rights from us, could materially harm our business, financial condition and results of operations.

We rely on third parties to conduct our preclinical and clinical trials. If these third parties do not successfully perform their contractual legal and regulatory duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third-party medical institutions, clinical investigators, contract laboratories and other third-party CROs to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the member states of the EEA and comparable foreign regulatory authorities for all of our products in clinical development.

Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA 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 by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether they devote sufficient time and resources to our on-going clinical, nonclinical and preclinical programs. If CROs 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 clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If the third parties conducting our GCP preclinical studies or our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to our clinical trial protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. Switching or adding CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

Risks Related to Our Business and Industry

The COVID-19 pandemic or other pandemics, epidemics or outbreaks of an infectious disease may materially and adversely impact our business, including our preclinical studies and clinical trials.

The COVID-19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce.

As a result of the COVID-19 pandemic, outbreaks from variants of COVID-19, or other pandemics, epidemics or outbreaks of infectious disease, we may experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of health care 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 governments, employers and others, or interruption of clinical trial subject visits and study procedures, 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 contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in preclinical studies due to restricted or limited operations resulting from restrictions on our on-site activities;
- 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;
- impacts from prolonged remote work arrangements, such as strains on our business continuity plans, cybersecurity risks, and inability of certain employees to perform their work remotely; and
- interruption or delays to our sourced discovery and clinical activities.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain. If we or any of the third parties with whom we engage were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. Additionally, concerns over the economic impact of COVID-19 pandemic have caused extreme volatility in financial and other capital markets, which has and may continue to adversely impact our stock price and our ability to access capital markets.

We will need to increase the size of our organization and the scope of our outside vendor relationships, and we may experience difficulties in managing growth.

In addition to our employees, we have access to certain of BioXcel LLC's employees and resources through the various agreements we have with BioXcel LLC. We have been expanding our management team to include an operational ramp up of additional technical staff required to achieve our business objectives. We will need to continue to expand our managerial, commercial, operational, technical, and scientific, financial, and other resources to manage our operations and clinical trials, continue our research and development activities, and commercialize IGALMI and any approved product candidates. Our management and scientific personnel, systems, and facilities currently in place may not be adequate to support our future growth.

Our need to effectively manage our operations, growth and various projects requires that we:

- manage our clinical trials effectively, including our planned clinical trials of our current, and any future, product candidates;
- manage our internal development efforts effectively while carrying out our contractual obligations to licensors, contractors and other third parties;
- manage our commercial operations effectively;
- continue to improve our operational, financial and management controls and reporting systems and procedures; and
- attract and retain enough talented employees.

We may utilize the services of third-party vendors to perform tasks including preclinical and clinical trial management, statistics and analysis, regulatory affairs, medical advisory, market research, formulation development, chemistry, manufacturing and control activities, other drug development functions, legal, auditing, financial advisory, and investor relations. Our growth strategy may also entail expanding our group of contractors or consultants to implement these and other tasks going forward. Because we rely on numerous consultants, to outsource many key functions of our business, we will need to be able to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. However, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for our product candidate or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants 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 expanding our groups of consultants and contractors, we may be unable to successfully implement the tasks necessary to further develop and commercialize our product candidate and, accordingly, may not achieve our research, development, and commercialization goals.

We depend on our senior management team, and the loss of one or more of our executive officers or key employees or an inability to attract and retain highly skilled employees could adversely affect our business.

Our success depends largely upon the continued services of our key executive officers, Vimal Mehta, our Chief Executive Officer, President and a member of our Board, as well as the other principal members of our management, scientific, clinical teams and commercial readiness teams. We do not maintain “key person” insurance for any of these executive officers or any of our other key employees. We also rely on our leadership team in the areas of research and development, marketing, services and selling, general and administrative functions. We have been relying on our commercial readiness team in connection with the commercialization of IGALMI. From time to time, there may be changes in our executive management and leadership teams resulting from the hiring or departure of executives or other key employees, which could disrupt our business. The replacement of one or more of our executive officers or other key employees would likely involve significant time and costs and may significantly delay or prevent the achievement of our business objectives.

To continue to execute our growth strategy, we also must attract and retain highly skilled personnel. We might not be successful in maintaining our unique culture and continuing to attract and retain qualified personnel. We have, from time to time, had difficulty hiring and retaining highly skilled personnel with appropriate qualifications, and we have experienced increased costs to recruit such personnel. We expect to experience such difficulties in the future. The pool of qualified personnel with experience working within the biopharmaceutical and biotechnology market is limited overall. In addition, many of the companies with which we compete for experienced personnel have greater resources than we have.

In addition, in making employment decisions, particularly in the biotechnology and high-technology industries, job candidates often consider the value of the stock options or other equity instruments they are to receive in connection with their employment. Volatility in the price of our stock might, therefore, adversely affect our ability to attract or retain highly skilled personnel. Furthermore, the requirement to expense the fair value of stock options and other equity

instruments might discourage us from granting the size or type of stock option or equity awards that job candidates require to join our Company. If we fail to attract new personnel or fail to retain and motivate our current personnel, our business and future growth prospects could be severely harmed.

We may acquire other companies or technologies, which could divert our management's attention, result in dilution to our stockholders and otherwise disrupt our operations and adversely affect our operating results.

We may in the future seek to acquire or invest in businesses, applications and services or technologies that we believe could complement or expand our services, enhance our technical capabilities or otherwise offer growth opportunities. The pursuit of potential acquisitions may divert the attention of management and cause us to incur various expenses in identifying, investigating and pursuing suitable acquisitions, whether or not they are consummated.

In addition, we do not have any experience in acquiring other businesses. If we acquire additional businesses, we may not be able to integrate the acquired personnel, operations and technologies successfully, or effectively manage the combined business following the acquisition. We also may not achieve the anticipated benefits from the acquired business due to a number of factors, including:

- inability to integrate or benefit from acquired technologies or services in a profitable manner;
- unanticipated costs or liabilities associated with the acquisition;
- difficulty integrating the accounting systems, operations and personnel of the acquired business;
- difficulties and additional expenses associated with supporting legacy products and hosting infrastructure of the acquired business;
- difficulty converting the customers of the acquired business onto our platform and contract terms, including disparities in the revenue, licensing, support or professional services model of the acquired company;
- diversion of management's attention from other business concerns;
- adverse effects to our existing business relationships with business partners and customers as a result of the acquisition;
- the potential loss of key employees;
- use of resources that are needed in other parts of our business; and
- use of substantial portions of our available cash to consummate the acquisition.

In addition, a significant portion of the purchase price of companies we acquire may be allocated to acquired goodwill and other intangible assets, which must be assessed for impairment at least annually. In the future, if our acquisitions do not yield expected returns, we may be required to take charges to our operating results based on this impairment assessment process, which could adversely affect our results of operations.

Acquisitions could also result in dilutive issuances of equity securities or the incurrence of debt, which could adversely affect our operating results. In addition, if an acquired business fails to meet our expectations, our operating results, business, and financial position may suffer.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with any regulations applicable to us, to provide accurate information to regulatory authorities, to comply with manufacturing standards we have established, to comply with federal and state health care fraud and abuse laws and regulations, or to report financial information or data accurately or disclose unauthorized

activities to us. In particular, 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. Employee misconduct could also involve the improper use of information obtained during clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risk.

Business interruptions could adversely affect future operations, revenues, and financial conditions, and may increase our costs and expenses.

Our operations, and those of our directors, advisors, contractors, consultants, CROs, and collaborators, could be adversely affected by earthquakes, floods, hurricanes, typhoons, extreme weather conditions, fires, water shortages, power failures, business systems failures, medical epidemics, pandemics such as the COVID-19 pandemic, and other natural and man-made disaster or business interruptions. Our phones, electronic devices and computer systems and those of our directors, advisors, contractors, consultants, CROs, and collaborators are vulnerable to damages, theft and accidental loss, negligence, unauthorized access, terrorism, war, electronic and telecommunications failures, and other natural and man-made disasters. Several of our employees conduct business outside of our headquarters and leased or owned facilities. These locations may be subject to additional security and other risk factors due to the limited control of our employees. If such an event as described above were to occur in the future, it may cause interruptions in our operations, delay research and development programs, clinical trials, regulatory activities, manufacturing and quality assurance activities, sales and marketing activities, hiring, training of employees and persons within associated third parties, and other business activities. 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 data.

Likewise, we will rely on third parties, including ARx, to manufacture IGALMI and our product candidates and to conduct clinical trials, and similar events as those described in the prior paragraph relating to their business systems, equipment and facilities could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed or altogether terminated.

Data breaches or cyber-attacks could disrupt our business operations and information technology systems or those of third parties on which we rely, adversely impact our financial results, or result in the loss or exposure of confidential or sensitive product candidate, clinical trial, employee, or Company information.

Our information technology systems and those of third parties on which we rely have been and may in the future be attacked or breached by individuals or organizations intending to obtain sensitive data regarding our business, our product candidates, clinical trials or other third parties with whom we do business; harm or disrupt our business operations; or otherwise misappropriate information or Company funds. A security compromise of our information technology systems or business operations, or those of third parties on which we rely, could occur through a variety of methods such as from cyber-attacks and cyber-intrusions over the Internet, malware, computer viruses, email spoofing, attachments to e-mails, persons inside or outside our organization or persons with access to systems inside our organization. The risk of such intrusions, threats to data and information technology systems and breaches has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We use our information technology systems to protect confidential or sensitive product candidate, clinical trial, employee, and Company information.

Any attack on such systems that results in disruptions to our operations or the unauthorized release or loss of such information could have a material adverse effect on our business reputation, increase our costs and expose us to material legal claims and liability. If the unauthorized release or loss of product candidate, clinical trial, employee or other confidential or sensitive data were to occur, our operations and financial results and our share price could be adversely affected.

While we maintain some of our own critical information technology systems, we also depend on third parties to provide important information technology services relating to several key business functions. Our measures to prevent, detect and mitigate these threats, including password protection, firewalls, backup servers, threat monitoring and periodic penetration testing, may not be successful in preventing a data breach or limiting the effects of a breach. 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 may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. Furthermore, the security measures employed by third-party service providers may prove to be ineffective at preventing breaches of their systems. Although we maintain insurance for our business, the coverage under our policies may not be adequate to compensate us for all losses that may occur.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards, and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the U.S. and abroad. Additionally, our use of AI and machine learning may be subject to laws and evolving regulations regarding the use of AI or machine learning, controlling for data bias, and anti-discrimination. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer, use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state, or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance, and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission, and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. If we are determined to act as a covered entity or business associate under HIPAA and be directly regulated under HIPAA, any person acting on our behalf may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In addition, the CCPA went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with data breach litigation. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states in the U.S. Further, the CPRA generally went into effect in January 2023, and significantly amends CCPA, imposing additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in

increased privacy and information security enforcement. Additional compliance investment and potential business process changes may be required. If we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In Europe, the GDPR went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the U.S., in July 2020, the Court of Justice of the EU ("CJEU") limited how organizations could lawfully transfer personal data from the EU/EEA to the U.S. by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses ("SCCs"). In March 2022, the U.S. and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 2020 have taken a restrictive approach to international data transfers. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Further, from January 1, 2021, companies had to comply with the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR (i.e., fines up to the greater of £17,500 or 4% of global turnover).

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

Increased scrutiny of and evolving expectations for environmental, social and governance ("ESG") initiatives may impose additional costs or otherwise adversely impact our business.

There has been an increased focus from investors, capital providers, shareholder advocacy groups, other market participants, customers, and other stakeholder groups regarding companies' ESG initiatives. While we may at times engage in voluntary initiatives (such as voluntary disclosures, certifications, or goals, among others) or commitments to improve the ESG profile of our Company and/or offerings, such initiatives or achievements of such commitments may be costly and may not have the desired effect. Additionally, some investors may use third-party or proprietary ESG ratings to guide their investment strategies and, in some cases, may choose not to invest in us if they believe our ESG practices are inadequate. The criteria by which companies' ESG practices are assessed are evolving, which could result in greater expectations of us and cause us to undertake costly initiatives to satisfy such new criteria. Alternatively, if we elect not to or are unable to satisfy new criteria or do not meet the criteria, some investors may conclude that our policies with respect to ESG are inadequate and choose not to invest in us.

If our ESG practices do not meet evolving investor or other stakeholder expectations and our standards, reputation, ability to attract or retain employees and desirability as an investment or business partner could be negatively impacted. Similarly, our failure or perceived failure to adequately pursue or fulfill any ESG goals and objectives or to satisfy various reporting standards, if any, could expose us to additional regulatory, social or other scrutiny, the imposition of

unexpected costs, or damage to our reputation, which in turn could have a material adverse effect on our business and could cause the market value of our common stock to decline.

Our failure to successfully acquire, develop and market additional product candidates or approved drug products could impair our ability to grow.

As part of our growth strategy, we may evaluate, acquire, license, develop and/or market third-party products or product candidates and technologies. Our internal research capabilities are limited and we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select and acquire promising pharmaceutical product candidates and products. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's and technical personnel's time and attention to develop acquired products or technologies;
- incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we acquire will be manufactured profitably or achieve market acceptance.

Our ability to use our net operating losses and tax credits to offset future taxable income and income tax liabilities maybe limited.

As of December 31, 2022, the Company had federal net operating loss carryforwards ("NOLs") of approximately $222.4 million and state NOLs of approximately $214.5 million. If not utilized, the federal and state NOLs, which are subject to expiration, will begin to expire in 2037. Federal NOLs generated in taxable years beginning after December 31, 2017, may be carried forward indefinitely but may only be used to offset 80% of our taxable income in future taxable years beginning after December 31, 2020. As of December 31, 2022, we also had approximately $10.0 million of federal orphan drug credits and research and development credits, or tax credits, which will begin to expire in 2037 if not

utilized. The utilization of such NOLs and tax credits and realization of tax benefits in future years depends upon our having taxable income and income tax liabilities.

In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-ownership change NOLs and tax credits to offset future taxable income or income tax liabilities. For these purposes, an ownership change generally occurs where the aggregate change in stock ownership, of one or more stockholders or groups of stockholders owning at least 5% of a corporation's stock, exceeds 50 percentage points over a rolling three-year period. We may have experienced ownership changes in the past, and future changes in our stock ownership, many of which are outside of our control, could result in ownership changes in the future. Our state NOLs or tax credits may also be impaired under state law. Accordingly, even if we attain profitability, we may not be able to utilize a material portion of our NOLs or tax credits. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Risks Related to Our Intellectual Property

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection. If our patent position does not adequately protect our product candidates, others could compete against us more directly, which would harm our business, possibly materially.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future approved products and product candidates, the processes used to manufacture them and the methods for using them, as well as successfully defending these patents against third-party challenges. We are the owner of record of patents and patent applications pending in the U.S. and in certain foreign jurisdictions. Patents issued from non-provisional applications, which are typically filed from provisional patent applications or from PCT applications that enter the national phase. Neither provisional patent applications nor PCT applications issue directly as patents. We own PCT patent applications relating to our platform technologies covering methods of use and applications of the platform technologies.

We cannot be certain that any future patents will issue with claims that cover our product candidates. Our ability to stop third parties from making, using, selling, offering to sell, or importing our 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 positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the U.S. or in foreign jurisdictions outside of the U.S. Changes in either the patent laws or interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that may be issued from the applications we currently, or may in the future, own or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical, or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third-party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition, reexamination, review, reissue, post grant review or invalidity proceedings before U.S. or non-U.S. patent offices.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make compounds that are similar to our product candidates, but that are not covered by the claims of our patents;

- we might not have been the first to make the inventions covered by our pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- our pending patent applications may not result in issued patents;
- the claims of our issued patents or patent applications when issued may not cover our products or product candidates;
- any patents that we obtain may not provide us with any competitive advantages;
- any granted patents may be held invalid or unenforceable as a result of legal challenges by third parties; and
- the patents of others may have an adverse effect on our business.

Obtaining and maintaining 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 for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our owned and in-licensed patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with various procedural, document submission, fee payment and other requirements 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 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, potential competitors might be able to enter the market with similar or identical products or technology. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

We may be required to enter into intellectual property license agreements that are important to our business. These license agreements may impose various diligence, milestone payment, royalty, and other obligations on us. For example, we may enter into exclusive license agreements with various universities and research institutions, we may be required to use commercially reasonable efforts to engage in various development and commercialization activities with respect to licensed products and may need to satisfy specified milestone and royalty payment obligations. If we fail to comply with any obligations under our agreements with any of these licensors, we may be subject to termination of the license agreement in whole or in part; increased financial obligations to our licensors or loss of exclusivity in a particular field or territory, in which case our ability to develop or commercialize products covered by the license agreement will be impaired.

In addition, disputes may arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our diligence obligations under the license agreement and what activities satisfy those obligations;

- if a third-party expresses interest in an area under a license that we are not pursuing, under the terms of certain of our license agreements, we may be required to sublicense rights in that area to a third-party, and that sublicense could harm our business; and

- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected approved products or product candidates.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly.

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

We or our licensors 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 or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants, or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets, or other intellectual property. If we or our licensors 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 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.

An NDA submitted under Section 505(b)(2) subjects us to the risk that we may be subject to a patent infringement lawsuit that would delay or prevent the review or approval of our product candidate.

Our product candidates have been or will be submitted to the FDA for approval under Section 505(b)(2) of the FDCA. Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from studies that were not conducted by, or for, the applicant and on which the applicant has not obtained a right of reference. The 505(b)(2) application would enable us to reference published literature and/or the FDA's previous findings of safety and effectiveness for a branded reference drug with the same active ingredient. For NDAs submitted under Section 505(b)(2) of the FDCA, the patent certification and related provisions of the Hatch-Waxman Act apply. In accordance with the Hatch-Waxman Act, such NDAs may be required to include paragraph IV certifications that certify that any patents listed in the FDA's Orange Book, with respect to any product referenced in the 505(b)(2) application, are invalid, unenforceable or will not be infringed by the manufacture, use or sale of the product that is the subject of the 505(b)(2) NDA.

Under the Hatch-Waxman Act, the holder of patents that the 505(b)(2) application references may file a patent infringement lawsuit after receiving notice of the paragraph IV certification. Filing of a patent infringement lawsuit against the filer of the 505(b)(2) applicant within 45 days of the patent owner's receipt of notice triggers a one-time, automatic, 30-month stay of the FDA's ability to approve the 505(b)(2) NDA, unless patent litigation is resolved in the favor of the paragraph IV certification filer, or the patent expires before that time. Accordingly, we may invest a significant amount of time and expense in the development of one or more product candidates only to be subject to significant delay and patent litigation before such product candidates may be commercialized, if at all. In addition, a 505(b)(2) application will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the branded reference drug product has expired. The FDA may also require us to perform one or more additional clinical studies or measurements to support the change from the branded reference drug, which could be time consuming and could substantially delay our achievement of regulatory approvals for such product candidates. The FDA may also reject our future 505(b)(2) submissions and require us to file such

submissions under Section 505(b)(1) of the FDCA, which would require us to provide extensive data to establish safety and effectiveness of the drug product for the proposed use and could cause delay and be considerably more expensive and time consuming. These factors, among others, may limit our ability to successfully commercialize our product candidates.

We may incur substantial costs as a result of litigation or other proceedings relating to patents and other intellectual property rights.

If we choose to commence a proceeding or litigation to prevent another party from infringing our patents, that party will have the right to ask the examiner or court to rule that our patents are invalid or should not be enforced against them. There is a risk that the examiner or court will decide that our patents are not valid and that we do not have the right to stop the other party from using the related inventions. There is also the risk that, even if the validity of our patents is upheld, the examiner or court will refuse to stop the other party on the ground that such other party's activities do not infringe our rights to such patents. In addition, the U.S. Supreme Court has recently modified some tests used by the USPTO in granting patents over the past 20 years, which may decrease the likelihood that we will be able to obtain patents and increase the likelihood of challenge to any patents we obtain or license. Any proceedings or litigation to enforce our intellectual property rights or defend ourselves against claims of infringement of third-party intellectual property rights could be costly and divert the attention of managerial and scientific personnel, regardless of whether such litigation is ultimately resolved in our favor. We may not have sufficient resources to bring these actions to a successful conclusion. Moreover, if we are unable to successfully defend against claims that we have infringed the intellectual property rights of others, we may be prevented from using certain intellectual property and may be liable for damages, which in turn could materially adversely affect our business, 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, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates.

Our success will depend in part on our ability to operate without infringing, misappropriating, or otherwise violating the proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our products, or the manufacture or use of our product candidates, including interference proceedings, post grant review, inter partes review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions. The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. The costs of these lawsuits could affect our results of operations and divert the attention of managerial and scientific personnel. Some of these third parties may be better capitalized and have more resources than us. There is a risk that a court would decide that we are infringing the third-party's patents and would order us to stop the activities covered by the patents. In that event, we may not have a viable way around the patent and may need to halt commercialization of the relevant product candidate. In addition, there is a risk that a court will order us to pay the other party damages for having violated the other party's patents. In addition, we may be obligated to indemnify our licensors and collaborators against certain intellectual property infringement claims brought by third parties, which could require us to expend additional resources. The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform.

If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the U.S., proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing

technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates.

We cannot be certain that others have not filed patent applications for technology covered by our pending applications, or that we were the first to invent the technology, because:

- some patent applications in the U.S. may be maintained in secrecy until the patents are issued;
- patent applications in the U.S. are typically not published until 18 months after the priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours. Any such patent application may have priority over our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed U.S. patent applications on inventions similar to ours that claim priority to any applications filed prior to the priority dates of our applications, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the U.S. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar inventions prior to our own inventions, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications and may be entitled to priority over our applications in such jurisdictions.

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.

If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our technology and products could be significantly diminished.

We also rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Furthermore, any license agreements we enter into in the future may require us to notify, and in some cases license back to the licensor, certain additional proprietary information or intellectual property that we developed using the rights licensed to us under these agreements. Any such licenses back to the licensor could allow our licensors to use that proprietary information or intellectual property in a manner that could harm our business. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its transparency initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed alleged trade secrets.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed trade secrets or other

proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we could lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Our intellectual property may not be sufficient to protect our products from competition, which may negatively affect our business as well as limit our partnership or acquisition appeal.

We may be subject to competition despite the existence of intellectual property we license or own. We can give no assurances that our intellectual property claims will be sufficient to prevent third parties from designing around patents we own or license and developing and commercializing competitive products. The existence of competitive products that avoid our intellectual property could materially adversely affect our operating results and financial condition. Furthermore, limitations, or perceived limitations, in our intellectual property may limit the interest of third parties to partner, collaborate or otherwise transact with us, if third parties perceive a higher than acceptable risk to commercialization of our products or future products.

Our drug re-innovation approach involves the filing of patent applications covering new methods of use and/or new formulations of previously known, studied and/or marketed drugs. Although the protection afforded by our patent and patent applications may be significant with respect to BXCL501, BXCL502, BXCL701 and BXCL702, when looking at our patents' ability to block competition, the protection offered by our patents may be, to some extent, more limited than the protection provided by patents claiming the composition of matter of entirely new chemical structures previously unknown. If a competitor were able to successfully design around any method of use and formulation patents we may have in the future, our business and competitive advantage could be adversely affected.

We may elect to sue a third-party, or otherwise make a claim, alleging infringement or other violation of patents, trademarks, trade dress, copyrights, trade secrets, domain names or other intellectual property rights that we either own or license from BioXcel LLC. If we do not prevail in enforcing our intellectual property rights in this type of litigation, we may be subject to:

- paying monetary damages related to the legal expenses of the third-party;
- facing additional competition that may have a significant adverse effect on our product pricing, market share, business operations, financial condition, and the commercial viability of our products; and
- restructuring our company or delaying or terminating select business opportunities, including, but not limited to, research and development, clinical trial, and commercialization activities, due to a potential deterioration of our financial condition or market competitiveness.

A third-party may also challenge the validity, enforceability, or scope of the intellectual property rights that we license or own; and the result of these challenges may narrow the scope or claims of or invalidate patents that are integral to our product candidates in the future. There can be no assurance that we will be able to successfully defend patents we own in an action against third parties due to the unpredictability of litigation and the high costs associated with intellectual property litigation, amongst other factors.

Intellectual property rights and enforcement may be less extensive in jurisdictions outside of the U.S.; thus, we may not be able to protect our intellectual property and third parties may be able to market competitive products that may use some, or all, of our intellectual property.

Changes to patent law, including the Leahy-Smith America Invents Act of 2011 and the Patent Reform Act of 2009 and other future article of legislation, may substantially change the regulations and procedures surrounding patent applications, issuance of patents, and prosecution of patents. We can give no assurances that our patents and those of our licensor, BioXcel LLC, can be defended or will protect us against future intellectual property challenges, particularly as they pertain to changes in patent law and future patent law interpretations.

In addition, enforcing and maintaining our intellectual property protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by the USPTO, courts and foreign

government patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements.

Risks Related to Owning our Common Stock

The price of our common stock may fluctuate substantially.

You should consider an investment in our common stock to be risky, and you should invest in our common stock only if you can withstand a significant loss and wide fluctuations in the market value of your investment. Some factors that may cause the market price of our common stock to fluctuate, in addition to the other risks mentioned in this "Risk Factors" section, are:

- sale of our common stock by our stockholders, executives, and directors;
- volatility and limitations in trading volumes of our shares of common stock;
- speculative trading in and short sales of our stock, as well as trading phenomena such as the “short squeeze” and “short and distort” schemes;
- our ability to obtain financings to conduct and complete research and development activities including, but not limited to, our clinical trials, and other business activities;
- possible delays in the expected recognition of revenue due to lengthy and sometimes unpredictable sales timelines;
- the timing and success of introductions of new applications and services by us or our competitors or any other change in the competitive dynamics of our industry, including consolidation among competitors, customers or strategic partners;
- network outages or security breaches;
- our ability to attract new customers;
- customer renewal rates and the timing and terms of customer renewals;
- our ability to secure resources and the necessary personnel to conduct clinical trials on our desired schedule;
- commencement, enrollment or results of our clinical trials for our product candidates or any future clinical trials we may conduct;
- changes in the development status of our product candidates;
- any delays or adverse developments or perceived adverse developments with respect to the FDA’s review of our planned preclinical and clinical trials;
- any delay in our submission for studies or product approvals or adverse regulatory decisions, including failure to receive regulatory approval for our product candidates;
- unanticipated safety concerns related to the use of our product candidates;
- failures to meet external expectations or management guidance;
- changes in our capital structure or dividend policy, future issuances of securities, sales of large blocks of common stock by our stockholders;
- our cash position;

- announcements and events surrounding financing efforts, including debt and equity securities;
- our inability to enter into new markets or develop new products;
- reputational issues;
- competition from existing technologies and products or new technologies and products that may emerge;
- announcements of acquisitions, partnerships, collaborations, joint ventures, new products, capital commitments, or other events by us or our competitors;
- changes in general economic, political and market conditions in or any of the regions in which we conduct our business;
- changes in industry conditions or perceptions;
- changes in valuations of similar companies or groups of companies;
- analyst research reports, recommendation and changes in recommendations, price targets, and withdrawals of coverage;
- departures and additions of key personnel;
- disputes and litigations related to intellectual properties, proprietary rights, and contractual obligations;
- changes in applicable laws, rules, regulations, or accounting practices and other dynamics; and
- other events or factors, many of which may be out of our control.

In addition, if the market for stocks in our industry or industries related to our industry, or the stock market in general, experiences a loss of investor confidence, the trading price of our common stock could decline for reasons unrelated to our business, financial condition, and results of operations. If any of the foregoing occurs, it could cause our stock price to fall and may expose us to lawsuits that, even if unsuccessful, could be costly to defend and a distraction to management.

Because certain of our stockholders control a significant number of shares of our common stock, they may have significant influence over actions requiring stockholder approval.

As of December 31, 2022, our directors, executive officers and BioXcel LLC, and their respective affiliates, beneficially owned approximately 37% of our outstanding shares of common stock. As a result, these stockholders, acting together, would have significant control over the outcome of matters submitted to our stockholders for approval, including the election of directors and any merger, consolidation, or sale of all, or substantially all, of our assets. In addition, these stockholders, acting together, would have significant control over the management and affairs of our company. Accordingly, this concentration of ownership might harm the market price of our common stock by:

- delaying, deferring or preventing a change in corporate control;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

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

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. Any return to stockholders will therefore be limited to the increase, if any, of our share price.

If we were deemed to be an investment company under the Investment Company Act of 1940, as amended (the "1940 Act"), applicable restrictions could make it impractical for us to continue our business as contemplated and could have a material adverse effect on our business, financial condition, and results of operations.

Under Sections 3(a)(1)(A) and (C) of the 1940 Act, a company generally will be deemed to be an "investment company" for purposes of the 1940 Act if (1) it is, or holds itself out as being, engaged primarily, or proposes to engage primarily, in the business of investing, reinvesting or trading in securities or (2) it engages, or proposes to engage, in the business of investing, reinvesting, owning, holding or trading in securities and it owns or proposes to acquire investment securities having a value exceeding 40% of the value of its total assets (exclusive of U.S. government securities and cash items) on an unconsolidated basis. We do not believe that we are an "investment company," as such term is defined in the 1940 Act.

Notwithstanding Sections 3(a)(1)(A) and (C) of the 1940 Act, we are a research and development company and comply with the safe harbor requirements of Rule 3a-8 of the 1940 Act. We intend to conduct our operations so that we will not be deemed an investment company. However, if we were to be deemed an investment company, restrictions imposed by the 1940 Act, including limitations on our capital structure and our ability to transact with affiliates, could make it impractical for us to continue our business as contemplated and could have a material adverse effect on our business, financial condition, and results of operations.

We are an "emerging growth company" and "smaller reporting company" and are able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies, which could make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act") and we intend to take advantage of certain 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(b) of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In addition, Section 107 of the JOBS Act also provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act, for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We are not electing to delay such adoption of new or revised accounting standards, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. 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. We may take advantage of these reporting exemptions until we are no longer an "emerging growth company." We will remain an "emerging growth company" until December 31, 2023.

We are also a smaller reporting company, and we will remain a smaller reporting company until, as of fiscal year end, we determine that either (1) our annual revenues are at least $100 million and our voting and non-voting common stock held by non-affiliates is at least $250 million measured on the last business day of our most recent second fiscal quarter, or (2) our voting and non-voting common stock held by non-affiliates is at least $700 million measured on the last business day of our most recent second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, and have certain other reduced disclosure obligations, including,

among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We have elected to take advantage of certain of the reduced reporting obligations. We cannot predict whether investors will find our common stock less attractive if we 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 reduced or more volatile.

We may be at risk of securities class action litigation.

We may be at risk of securities class action litigation. In the past, biotechnology and pharmaceutical companies have experienced significant stock price volatility, particularly when associated with binary events such as clinical trials and product approvals. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business and result in a decline in the market price of our common stock.

Our certificate of incorporation, our bylaws, and Delaware law may have anti-takeover effects that could discourage, delay, or prevent a change in control, which may cause our stock price to decline.

Our amended and restated certificate of incorporation, our amended and restated bylaws and Delaware law could make it more difficult for a third-party to acquire us, even if closing such a transaction would be beneficial to our stockholders. We are authorized to issue up to 10 million shares of preferred stock. This preferred stock may be issued in one or more series, the terms of which may be determined at the time of issuance by our board of directors without further action by stockholders. The terms of any series of preferred stock may include voting rights (including the right to vote as a series on particular matters), preferences as to dividend, liquidation, conversion and redemption rights and sinking fund provisions. No preferred stock is currently outstanding. The issuance of any preferred stock could materially adversely affect the rights of the holders of our common stock, and therefore, reduce the value of our common stock. In particular, specific rights granted to future holders of preferred stock could be used to restrict our ability to merge with, or sell our assets to, a third-party and thereby preserve control by the present management.

Provisions of our amended and restated certificate of incorporation and our amended and restated bylaws and Delaware law also could have the effect of discouraging potential acquisition proposals or making a tender offer or delaying or preventing a change in control, including changes a stockholder might consider favorable. Such provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. In particular, the certificate of incorporation and bylaws and Delaware law, as applicable, among other things:

- provide the board of directors with the ability to alter the bylaws without stockholder approval;
- place limitations on the removal of directors;
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings; and
- provide that vacancies on the board of directors may be filled by a majority of directors in office, although less than a quorum.

Financial reporting obligations of being a public company in the U.S. are expensive and time-consuming, and our management is required to devote substantial time to compliance matters.

As a publicly traded company we have incurred and will continue to incur significant legal, accounting and other expenses. The obligations of being a public company in the U.S. require significant expenditures and place significant demands on our management and other personnel, including costs resulting from public company reporting obligations under the Exchange Act and the rules and regulations regarding corporate governance practices, including those under the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, and the listing requirements of the stock exchange on which our securities are listed. These rules require the establishment and maintenance of effective disclosure and financial controls and procedures, internal control over financial reporting and changes in corporate governance practices, among many other complex rules that are often difficult to implement, monitor and

maintain compliance with. Moreover, despite reforms made possible by the JOBS Act, the reporting requirements, rules, and regulations will make some activities more time-consuming and costly, particularly after we are no longer an "emerging growth company" beginning December 31, 2023. In addition, we expect these and similar 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 such insurance. Our continued compliance with applicable requirements and to keep pace with new regulations requires management and other personnel to devote a substantial amount of their time, otherwise we may fall out of compliance and risk becoming subject to litigation or being delisted, among other potential problems.

General Risk Factors

If securities or industry analysts do not publish research or reports, or publish unfavorable research or reports about our business, our stock price and trading volume may decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us, our business, our markets, and our competitors. We do not control these analysts. If securities analysts do not cover our common stock, the lack of research coverage may adversely affect the market price of our common stock. Furthermore, if one or more of the analysts who do cover us downgrade our stock or if those analysts issue other unfavorable commentary about us or our business, our stock price would likely decline. If one or more of these analysts cease coverage of us or fails to regularly publish reports on us, we could lose visibility in the market and interest in our stock could decrease, which in turn could cause our stock price or trading volume to decline and may also impair our ability to expand our business with existing customers and attract new customers.

Future sales and issuances of our common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations, including increased marketing, hiring new personnel, commercializing our products, and continuing activities as an operating public company. 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. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

If we fail to comply with the rules under the Sarbanes-Oxley Act related to accounting controls and procedures in the future, or, if we discover material weaknesses and other deficiencies in our internal control and accounting procedures, our stock price could decline significantly and raising capital could be more difficult.

Section 404 of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting. If we fail to comply with the rules under the Sarbanes-Oxley Act related to disclosure controls and procedures in the future, or, if we discover material weaknesses and other deficiencies in our internal control and accounting procedures, our stock price could decline significantly and raising capital could be more difficult. We have discovered material weaknesses in the past. If future material weaknesses or significant deficiencies are discovered or if we otherwise fail to achieve and maintain the adequacy of our internal control, we may not be able to ensure that we can conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to helping prevent financial fraud. If we cannot provide reliable financial reports or prevent fraud, our business and operating results could be harmed, investors could lose confidence in our reported financial information, and the trading price of our common stock could drop significantly.

Comprehensive tax reform bills could adversely affect our business and financial condition.

In 2017, the U.S. government enacted comprehensive federal income tax legislation that includes significant changes to the taxation of business entities. These changes include, among others, a permanent reduction to the corporate

income tax rate. Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and financial condition could be adversely affected. Future changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of any foreign earnings, and the deductibility of expenses under future reform legislation could have a material impact on the value of our deferred tax assets, could result insignificant one-time charges, and could increase our future U.S. tax expense.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters are located at 555 Long Wharf Drive in New Haven, Connecticut. The Company occupies 18,285 square feet of space. The leases for this space expire in February 2026 and we have a renewal option for one additional five-year term. We believe that our existing facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Item 3. Legal Proceedings

From time to time, we may be subject to litigation and claims arising in the ordinary course of business. We are not currently a party to any material legal proceedings, and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results, cash flows or financial condition.

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

Our common stock is traded on The Nasdaq Capital Market® under the symbol "BTAI."

Stockholders

As of March 13, 2023, there were 11 stockholders of record of our common stock. The actual number of holders of our common stock 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 or held by other nominees.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deems relevant.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 11. of Part III of this Annual Report on Form 10-K.

Unregistered Sales of Securities

None.

Issuer Purchases of Equity Securities

None.

Item 6. Reserved

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing elsewhere in this report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below, and those discussed in the section titled "Risk Factors" included elsewhere in this Annual Report on Form 10-K. All dollar amounts in the below Management's Discussion and Analysis of Financial Condition and Results of Operations are presented in U.S. dollars, and all dollar and share amounts are presented in thousands, unless otherwise noted or the context otherwise provides.

Overview

BioXcel Therapeutics, Inc. ("BTI" or the "Company") is a biopharmaceutical company utilizing artificial intelligence ("AI") approaches to develop transformative medicines in neuroscience and immuno-oncology. We are focused on utilizing cutting-edge technology and innovative research to develop high-value therapeutics aimed at transforming patients' lives. We employ a proprietary AI platform to reduce therapeutic development costs and potentially accelerate development timelines. Our approach leverages existing approved drugs and/or clinically evaluated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indications. We believe this differentiated approach has the potential to reduce the expense and time associated with drug development in diseases with substantial unmet medical needs.

On April 6, 2022, we announced that the United States ("U.S.") Food and Drug Administration ("FDA") approved IGALMI (dexmedetomidine or "Dex") sublingual film for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults. IGALMI is approved to be self-administrated by patients under the supervision of a health care provider. We deployed the first phase of our sales team for high priority targets in May 2022. Furthermore, on July 6, 2022, we announced that IGALMI was commercially available in doses of 120 and 180 microgram ("mcg") through the Company's third-party logistics provider and was available for order through wholesalers.

Our most advanced clinical development program is BXCL501, an investigational proprietary, orally dissolving film formulation of Dex for the treatment of agitation associated with psychiatric and neurological disorders.

We are conducting clinical trials for the at-home use of BXCL501 for agitation associated with bipolar disorders and schizophrenia. We also continue to conduct clinical trials evaluating BXCL501 for the acute treatment of agitation in Alzheimer's disease patients in residential care facilities and nursing homes and for adjunctive treatment of patients with Major Depressive Disorder ("MDD").

Our advanced immuno-oncology asset, BXCL701, is an investigational, oral innate immune activator currently being developed as a potential therapy for the treatment of aggressive forms of prostate cancer, pancreatic cancer and other solid and liquid tumors.

On April 19, 2022, we announced the formation of a wholly-owned subsidiary, OnkosXcel Therapeutics, LLC ("OnkosXcel"), to develop potentially transformative medicines in immuno-oncology. OnkosXcel is focused on the sustained expansion and optimization of our immuno-oncology franchise, while providing maximum strategic and financial flexibility. OnkosXcel plans to progress the development of BXCL701 and BXCL702. To support their development, we may pursue third-party investments in, or other strategic options for, OnkosXcel.

We continue to work closely with our clinical sites to monitor the potential impact of the evolving COVID-19 pandemic and the spread of its variants. To date, we have not experienced any significant delays in any of our ongoing or planned clinical trials, except for occasional COVID-19 related disruptions to our TRANQUILITY II and PLACIDITY trials. However, this could change rapidly.

IGALMI Commercial Progress

Since the commercial launch of IGALMI in July 2022, our commercial progress has yielded more than 65 formulary wins. Additionally, more than 600 hospital pharmacy and therapeutics ("P&T") committees are scheduled to review and

vote on IGALMI inclusion in their formularies over the next several months. In addition, nearly 50% of target beds are now under group purchasing organization ("GPO") contracts as of February 28, 2023. We are in active discussions with other leading GPOs. This has been primarily accomplished with our initial 26-person institutional sales force since our trade launch in July 2022.

We expanded our institutional sales force to 70 representatives in December 2022 to cover over 1,700 target hospitals as of February 28, 2023. During the fourth quarter of 2022, our Corporate Account Director team was focused on 59 high-volume, high-control integrated delivery network ("IDN") accounts. Formulary voting is currently scheduled for approximately 70,000 (25%) of our target IDN beds, with approximately 7,000 (2%) now approved.

We believe the value proposition for IGALMI will continue to evolve as we learn from market response. Staff shortages in the emergency departments ("EDs") of hospitals, complicated by the potential for staff injuries due to agitated patients, are becoming increasingly concerning to hospital administration. Due to limited agitation treatment options in the ED, intramuscular injection is often used. This approach can be both confrontational and coercive to agitated patients, often making their symptoms worse. Moreover, these patients may occupy ED beds for extended periods due to unresponsive sedation, reducing throughput and increasing costs. These conditions continue to reinforce the need for a drug with IGALMI's profile.

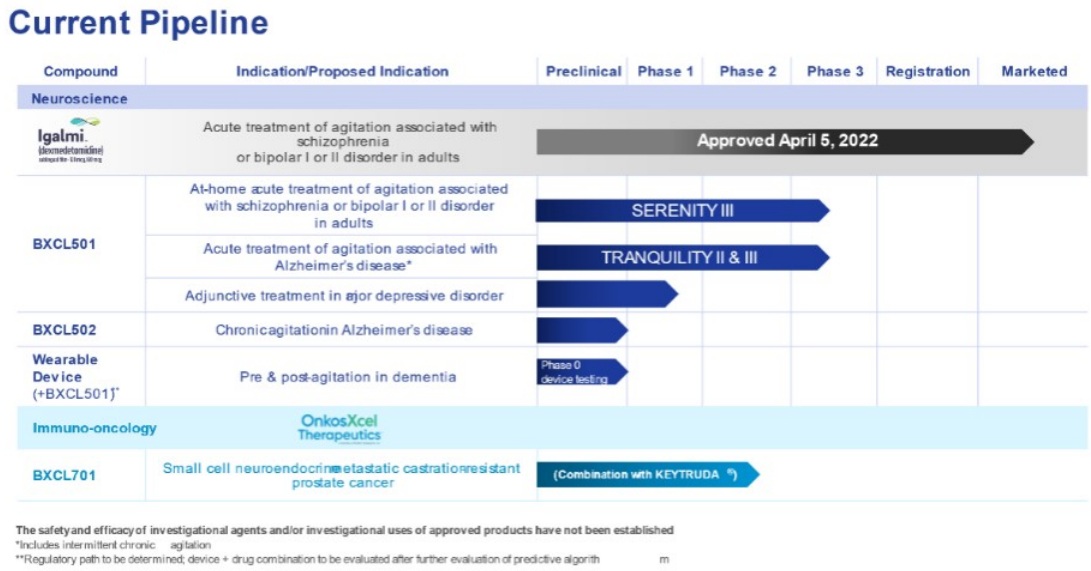
Our marketing efforts continue to drive awareness through an extensive convention presence, peer influence programs, and digital marketing campaigns. As of December 31, 2022, our peer-led IGALMI speaker programs have educated over 1,000 health care providers, while we have had over 350,000 web sessions on our branded health care provider website and additional touchpoints through other digital marketing efforts. With our sales team expansion and as we begin to garner additional P&T formulary adoption, we plan extensive digital and peer to peer marketing efforts in the first half of 2023 to continue to raise awareness, reinforce key messages and drive additional demand. In addition, we have planned promotional presence at leading national and regional conferences in 2023.

If IGALMI is approved outside the U.S., we would consider launching the product through collaborations with third parties.

Our continued commercialization efforts for IGALMI are designed to build the foundation to launch additional potential follow-on indications, if any, paving the way for our expanding neuroscience therapeutics business.

Our Clinical Programs

The following is a summary of the status of our major clinical development programs as of the date of this Annual Report on Form 10-K:



For additional information regarding our pipeline candidates, see Part I, Item 1, “Business” in this Annual Report on Form 10-K.

Basis of Presentation

The Company's consolidated financial statements are prepared in accordance with U.S. Generally Accepted Accounting Principles ("GAAP").

Components of Our Results of Operations

Product Revenues, Net

Revenues relate to sales of IGALMI from early product trials and reflects limited market access since commercial launch in July 2022. The revenues are net of rebates, chargebacks, discounts and other adjustments. During the fourth quarter of 2022, we began contracting directly with intermediaries such as GPOs.

Operating Costs and Expenses

Cost of Goods Sold

Cost of goods sold primarily relates to the costs of producing, packaging and delivering our product to customers.

Research and Development

Our research and development expenses reflect costs incurred for the research and development of our clinical and preclinical product candidates, which includes payments to BioXcel LLC. Research and development expenses primarily consist of salary, benefits and non-cash stock-based compensation for our research and development personnel, costs incurred under agreements with contract research organizations and sites that conduct our non-clinical studies and clinical trials, costs of outside consultants engaged in research and development activities, including their fees, non-cash stock-based compensation and travel expenses, the cost of acquiring, developing and manufacturing preclinical and clinical trial materials and lab supplies, and depreciation and other expenses.

We expense research and development costs as incurred.

Our research and development costs by program for the years ended December 31, 2022 and 2021 were as follows:

	Year ended December 31,	
	2022	2021
Direct external costs		
BXCL501	$ 52,044	$ 16,046
BXCL701	9,631	11,092
Other research and development programs	2,687	1,587
Total direct external costs	$ 64,362	$ 28,725
Internal personnel costs	22,831	21,282
Sub-total direct costs	$ 87,193	$ 50,007
Indirect costs and overhead	4,213	3,063
Research and development tax credit	(167)	(362)
Total research and development expenses	$ 91,239	$ 52,708

Selling, General and Administrative

Selling, general and administrative expenses primarily consist of salaries, benefits and non-cash stock-based compensation for our sales, executive and administrative personnel. Selling, general and administrative expenses also include legal expenses to pursue patent protection of our intellectual property, professional fees for audit and tax services and insurance charges.

We expect that our selling, general and administrative expenses will increase as we expand our clinical programs. We also expect increased selling, general and administrative costs resulting from our clinical trials, the continued commercialization of IGALMI and potential commercialization of our product candidates. We believe that these increases will likely include increased costs for liability insurance, hiring additional personnel to support future market research and current and future product commercialization efforts. In addition, we may also experience increased fees for outside consultants, attorneys, and accountants. We may also incur increased costs to comply with corporate governance, internal controls, investor relations and disclosures and similar requirements applicable to public companies.

Other Expense (Income)

Other expense (income) primarily consists of interest costs associated with the strategic financing facility the Company entered into in April 2022, changes in fair value of derivative financial instruments, and interest income earned on cash and cash equivalents that were comprised primarily of money market funds. We expect that interest expense will increase in the future, as we meet additional milestones and draw down additional funds under the strategic financing facility.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is set forth in Note 3 to the consolidated financial statements included in this Annual Report on Form 10-K.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

Product Revenues, Net

Product revenues, net for the year ended December 31, 2022, were $375, comprised of sales of IGALMI, subsequent to commercial launch in July 2022. Sales to date resulted from early product trials and reflect limited market access. There were no revenues in 2021.

Cost of Goods Sold

Cost of goods sold for the year ended December 31, 2022, were $20, which primarily related to the costs to produce, package and deliver IGALMI to customers. There were no cost of goods sold in 2021.

Research and Development Expense

Research and development expenses for the years ended December 31, 2022 and 2021 were as follows:

	Year ended December 31,			
	2022	2021	Change	% Change
Personnel and related costs	$ 18,272	$ 14,624	$ 3,648	25 %
Non-cash stock-based compensation	4,558	6,658	(2,100)	(32)%
Professional fees	14,342	11,932	2,410	20 %
Clinical trials expense	40,630	14,226	26,404	186 %
Chemical, manufacturing and controls cost	10,144	3,506	6,638	189 %
Travel and other costs	3,460	2,124	1,336	63 %
Research and development tax credit	(167)	(362)	195	54 %
Total research and development expenses	$ 91,239	$ 52,708	$ 38,531	73 %

The increase of $38,531 for the year ended December 31, 2022, relative to the same period in 2021 is primarily attributable to:

- An increase in personnel costs related to our efforts to grow our clinical team as we expanded our clinical trials, particularly evaluating BXCL501 for treatment of agitation in patients with Alzheimer's disease, as well as BXCL701 for treatment of prostate cancer.
- Increased professional fees due to required toxicology testing for IGALMI.
- An increase in clinical trials expenses due to the on-going TRANQUILITY II study of BXCL501 for the potential treatment of agitation in patients with Alzheimer's disease.
- Increased chemical, manufacturing and controls ("CMC") costs associated with producing materials related to testing required for IGALMI, as well as our clinical trials of BXCL501 for the treatment of agitation associated with Alzheimer's disease and BXCL701 for the treatment of prostate cancer.
- An increase in travel and other costs as we added personnel and increased site visits to pre-COVID-19 levels.

These increases were offset by a decrease in non-cash stock-based compensation, which was the result of lower grant date fair values for awards due to lower trading prices of the Company's common stock.

The State of Connecticut provides companies with the opportunity to exchange certain research and development credit carryforwards for cash in exchange for foregoing the carryforward of the research and development credit. The credit decreased in the year ended December 31, 2022 due to lower qualified spending in 2022 relative to 2021.

Following IGALMI's approval by the FDA, we capitalize costs related to commercial production of IGALMI as inventory and expense those CMC costs related to clinical trials.

Selling, General and Administrative Expense

Selling, general and administrative expenses for the years ended December 31, 2022 and 2021 were as follows:

	Year ended December 31,			
	2022	2021	Change	% Change
Personnel and related costs	$ 20,690	$ 9,576	$ 11,114	116 %
Non-cash stock-based compensation	12,779	12,798	(19)	(0)%
Professional fees	14,313	10,646	3,667	34 %
Commercial and marketing	13,006	16,070	(3,064)	(19)%
Insurance	2,370	2,136	234	11 %
Travel and other costs	5,603	3,001	2,602	87 %
Total selling, general and administrative expenses	$ 68,761	$ 54,227	$ 14,534	27 %

The increase of $14,534 for the year ended December 31, 2022, relative to the same period in 2021 is primarily attributable to:

- An increase in personnel and related costs due to our efforts to expand our functional teams, particularly in sales, for the commercial launch of IGALMI in the U.S.
- Increased professional fees, mainly for corporate legal fees, accounting and recruiting costs, primarily relating to the commercial launch of IGALMI in the U.S., formation of OnkosXcel, and higher operating support levels.
- An increase in travel and other costs as the Company resumed a more traditional travel schedule after restrictions relating to the COVID-19 pandemic were eased, and as a result of the commercial launch of

IGALMI. In addition, we experienced higher technology costs related to the addition of personnel and expansion of our operations.

These increases were offset by lower commercial and marketing costs due to reduced spending for market research and campaign development costs in 2022; we incurred higher market research and campaign development costs in 2021 in anticipation of the potential commercial launch of IGALMI.

Other Expense (Income)

Interest expense increased for 2022 relative to 2021 primarily due to borrowings under the OFA Facilities (defined subsequently herein) the Company entered into in April 2022. The expense was partially offset by interest income earned on cash and cash equivalents that were held primarily in short-term money market funds. Other expense, net is primarily associated with changes in fair value of derivative financial instruments for the period.

Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented. For a discussion of inflationary risks to our future revenues under the Inflation Reduction Act, see "*Health care reform measures could hinder or prevent our product candidates*' commercial success." in Part I, Item 1A., "Risk Factors" elsewhere in this Annual Report on Form 10-K.

Liquidity and Capital Resources

As of December 31, 2022, we had cash and cash equivalents of $193,725, working capital of $169,970 and stockholders' equity of $76,775. Net cash used in operating activities was $135,341 and $82,153 for the years ended December 31, 2022 and 2021, respectively. We incurred losses of approximately $165,757 and $106,931 for the years ended December 31, 2022 and 2021, respectively. We have generated limited revenues to date, and we have not yet achieved profitability. We expect that our research and development and selling, general and administrative expenses will continue to increase and, as a result, we will need to generate significant product revenues to achieve profitability. We believe that our current cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements for at least one year from the date of this Annual Report on Form 10-K.

We may obtain additional financing through sales of the Company's equity securities, third-party investments in or other strategic options for OnkosXcel, entering into strategic partnership arrangements and/or short-term borrowings from banks, stockholders or other related parties, if needed, or a combination of any of the foregoing. There are no assurances that we will be successful in obtaining an adequate level of financing as and when needed to finance our operations on terms acceptable to us or at all, particularly during when there is market uncertainty or an economic downturn. If we are unable to secure adequate additional funding as and when needed on acceptable or commercially reasonable terms, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more product candidates. In addition, there are various macro-economic trends affecting the financing markets whose impact on our liquidity and future funding requirements are uncertain as of the filing date of this Annual Report on Form 10-K. We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts. See "*Risks Related to Financial Position and Need for Additional Capital; We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.*" in Part I. Item 1A., "Risk Factors" elsewhere in this Annual Report on Form 10-K.

Sources of Liquidity

We have focused our efforts on raising capital and building the products in our pipeline, and only recently on launching sales for our first FDA approved product IGALMI. Since our inception, our operations have been financed primarily from proceeds from the sale of equity securities, including our initial public offering, private placements of our common stock, registered offerings of our common stock, an Open Market Sale Agreement (the "Sale Agreement") with Jefferies LLC ("Jefferies"), and borrowings under strategic financing arrangements (as described below). We have not

yet established an ongoing source of revenue sufficient to cover our operating costs and will need to do so in future periods.

In April 2022, we entered into two strategic financing agreements; a Credit Agreement and Guaranty (the "Credit Agreement") by and among the Company, as the borrower, certain subsidiaries of the Company from time to time party thereto as subsidiary guarantors, the lenders party thereto (the "Lenders"), and Oaktree Fund Administration LLC ("OFA") as administrative agent, and a Revenue Interest Financing Agreement (the "RIFA"; and together with the Credit Agreement, the "OFA Facilities") by and among the Company, the purchasers party thereto (the "Purchasers") and OFA as administrative agent. Pursuant to the Credit Agreement, the Lenders agreed to loan us up to $135,000 in senior secured term loans. On April 28, 2022, we borrowed the first tranche of $70,000 of loans. The remaining two tranches of the commitments under the Credit Agreement may be borrowed at our option prior to December 31, 2024 as follows:

- $35,000 upon satisfaction of certain conditions, including receipt of certain regulatory and financial milestones; and
- $30,000 upon satisfaction of certain conditions, including specified minimum net sales of the Company attributable to sales of BXCL501 for a trailing twelve consecutive month period.

The foregoing additional amounts were not eligible to be borrowed as of December 31, 2022.

Pursuant to the RIFA, the Purchasers agreed to provide us with up to $120,000 in financing for our near-term commercial activities of IGALMI, development and commercialization of BXCL501 and other general corporate purposes. On July 8, 2022, we drew down the first tranche of $30,000 under the RIFA. The remaining commitments under the RIFA may be drawn at our option prior to December 31, 2024, as follows:

- $45,000 payment upon satisfaction of certain conditions, including receipt of certain regulatory and patent related milestones and specified minimum net sales of BXCL501 during any consecutive twelve-month period; and
- $45,000 payment upon satisfaction of certain conditions, including receipt of certain regulatory and patent related milestones and specified minimum net sales of BXCL501 during any consecutive twelve-month period.

The foregoing additional amounts were not eligible to be borrowed as of December 31, 2022.

In connection with the Credit Agreement, we granted to the Lenders certain warrants to purchase up to 278 shares of our common stock, rights to purchase up to $5,000 of our common stock and warrants to purchase up to 175 individual ownership units (i.e., not in thousands) in OnkosXcel.

See Note 8, *Debt and Credit Facilities* in the Notes to Consolidated Financial Statements included in this Annual Report on Form 10-K for additional information relating to the Credit Agreement and RIFA, including applicable interest rates, payment obligations and certain restrictive and financial covenants thereunder. As of December 31, 2022, we were in compliance with all restrictive and financial covenants under the Credit Agreement and the RIFA.

In June 2021, we sold 3,155 shares of our common stock in a registered offering at a public offering price of $31.70 per share. We received proceeds of $96,937, net of issuance costs of $3,042.

In May 2021, we entered into the Sale Agreement with Jefferies pursuant to which we can offer and sell shares of our common stock, having an aggregate offering price of up to $100,000, from time to time, through an "at the market offering" program under which Jefferies will act as sale agent. We sold 124 shares under the Sale Agreement in June 2021 for proceeds of $4,056, net of issuance costs of $500. We did not sell any shares, and no proceeds were received under the Sale Agreement during the year ended December 31, 2022.

As of March 15, 2023, the Company sold 756 shares under the Sale Agreement with Jefferies in the first quarter of 2023 for net proceeds of $23,917, net of issuance costs of $740.

Cash Flows

	Year ended December 31,	
	2022	2021
Cash (used in) provided by:		
Operating activities	$ (135,341)	$ (82,153)
Investing activities	$ (139)	$ (445)
Financing activities	$ 96,237	$ 102,447

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $135,341 and was primarily attributable to our net loss of $165,757, a $1,985 increase in inventory of IGALMI and a $3,905 increase in prepaid expenses, other current assets and other assets, partially offset by $17,337 in non-cash stock-based compensation, a $4,611 increase in accrued and payment in kind interest, and $13,030 increase in accounts payable, accrued expenses and other current liabilities.

Net cash used in operating activities was $82,153 for the year ended December 31, 2021, and was primarily attributable to our $106,931 net loss and a $103 decrease in prepaid expense and other assets, partially offset by $19,455 in stock-based compensation and a $4,850 increase in accounts payable and accrued expenses.

Investing Activities

Cash used in investing activities for the year ended December 31, 2022, was $139 and was primarily attributable to the purchase of equipment and leasehold improvements.

Cash used in investing activities was $445 for the year ended December 31, 2021, and was attributable to the purchase of furniture and leasehold improvements.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2022, was $96,237 and was primarily attributable to $98,600 of proceeds received from the OFA Facilities, net of $2,646 of debt issuance costs.

Cash provided by financing activities was $102,447 for the year ended December 31, 2021, and was attributable to $96,937 in net proceeds from the issuance of common stock in our June 2021 public offering, $4,056 in net proceeds from the sale of common stock under the Sale Agreement with Jefferies and proceeds of $1,454 from the exercise of stock options.

Operating Capital and Capital Expenditure Requirements

We expect to continue to incur significant and increasing operating losses at least for the next several years as we commercialize IGALMI and as we expand our clinical trials of and seek marketing approval for BXCL501, BXCL502, BXCL701 and BXCL702, while pursuing development of additional product candidates. We expect to continue to incur net losses in the near term. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our planned clinical trials and our expenditures on other research and development activities.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect, and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development, and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. We anticipate that our expenses will increase substantially as we:

- continue our clinical development of our product candidates;
- conduct additional research and development with our product candidates;

- seek to identify, acquire, license, develop and commercialize product candidates;
- integrate acquired technologies into a comprehensive regulatory and product development strategy;
- maintain, expand and protect our intellectual property portfolio;
- hire scientific, clinical, quality control and administrative personnel;
- add operational, financial and management information systems and personnel, including personnel to support our drug development and commercial efforts;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- fully develop a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize IGALMI and any product candidates for which we may obtain regulatory approval; and
- continue to operate as a public company.

We believe that our existing cash and cash equivalents as of December 31, 2022, will be sufficient to enable us to fund operating expenses and capital expenditure requirements for at least the next 12 months from the date of the issuance of the consolidated financial statements included in this Annual Report on Form 10-K, including funding our ongoing research and development and commercialization efforts. We expect that we will need to obtain substantial additional funding to fund our ongoing operations. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interests of our existing stockholders may be materially diluted, and the terms of these securities could include liquidation or other preferences that could adversely affect the rights of our existing stockholders. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends, which could adversely impact our ability to conduct our business. If we are unable to raise capital when needed or on attractive terms, we could be forced to significantly delay, scale back or discontinue the development or commercialization of our product candidates, seek collaborators at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available, and relinquish or license, potentially on unfavorable terms, our rights to our product candidates that we otherwise would seek to develop or commercialize ourselves.

Contractual Obligations and Commitments

In April 2022, the Company signed a commercial supply agreement that requires minimum annual payments for the first three years of the agreement that in aggregate total $10,000 for the three-year period and the minimum commitment for 2023 is $3,000.

In February 2022, we signed a distribution agreement with a third-party to distribute product related to BXCL501 in the U.S. The distributor will be paid defined fees for its services under the agreement, which can be terminated by either party for cause. The distribution agreement can also be terminated by us without cause, subject to payment of agreed termination fees.

BTI leases office space for its corporate headquarters at 555 Long Wharf Drive, New Haven, Connecticut (the “HQ Lease”). The HQ Lease expires in February 2026. The Company has an option to renew the HQ Lease for one additional five-year term. Payments under the HQ Lease are fixed. The Company has approximately $1,209 of payments remaining under the HQ Lease. For additional details, see Note 12, *Leases* in the Notes to Consolidated Financial Statements included in this Annual Report on Form 10-K for additional information relating to the Company’s leases.

In addition, we are obligated to make quarterly interest and royalty payments under our Credit Agreement and RIFA, respectively. For additional details, see Note 8, *Debt and Credit Facilities* in the Notes to Consolidated Financial Statements included in this Annual Report on Form 10-K for additional information relating to the Company’s debt payment obligations.

Critical Accounting Policies and Estimates

The preparation of our consolidated financial statements in conformity with U.S. GAAP requires management to exercise its judgment. We exercise considerable judgment with respect to establishing sound accounting policies and in making estimates and assumptions that affect the reported amounts of our assets and liabilities, our recognition of revenues and expenses, and disclosure of commitments and contingencies at the date of the consolidated financial statements.

On an ongoing basis, we evaluate our estimates and judgments. We base our estimates and judgments on a variety of factors including our historical experience, knowledge of our business and industry, current and expected economic conditions, the attributes of our products and the regulatory environment. We periodically re-evaluate our estimates and assumptions with respect to these judgments and modify our approach when circumstances indicate that modifications are necessary.

While we believe that the factors we evaluate provide us with a meaningful basis for establishing and applying sound accounting policies, we cannot guarantee that the results will always be accurate. Since the determination of these estimates requires the exercise of judgment, actual results could differ from such estimates.

We define critical accounting policies as those that are reflective of significant judgments and uncertainty and which may potentially result in materially different results under different assumptions and conditions. In applying these critical accounting policies, our management uses its judgment to determine the appropriate assumptions to be used in making certain estimates. These estimates are subject to an inherent degree of uncertainty. Our critical accounting policies are noted below.

Stock Compensation

The Company has granted stock options, restricted stock units and profit units to employees, directors, and consultants, as well as warrants to other third parties. For employee, director and consultant awards, the value of each grant is estimated on the date of grant using a Black-Scholes option-pricing model. The Black-Scholes pricing model incorporates the volatility of the price of BTI's stock, the risk-free interest rate, the estimated life of the award, the closing market price of the Company's stock and the exercise price of the award. Management bases the Company's estimates of stock price volatility on the historical volatility of the Company's common stock, as well as a peer group of comparable companies. However, these estimates are neither predictive nor indicative of the future performance of the Company's stock. For purposes of the calculation, management assumed that no dividends would be paid during the life of the stock awards. The estimates utilized in the Black-Scholes calculation involve inherent uncertainties and the application of management judgment.

Research and Development Expenses

As part of the process of preparing the Company's consolidated financial statements, BTI's management is required to estimate prepaid and accrued expenses. This process involves reviewing open contracts, communicating with personnel to identify services that have been performed on behalf of the Company and estimating the level of service performed and the associated cost incurred for the service when BTI has not yet been invoiced or otherwise notified of the actual cost. The majority of the Company's service providers invoice BTI monthly for services performed or when contractual milestones are met. BTI management makes estimates of prepaid and/or accrued expenses as of each reporting date in the Company's consolidated financial statements based on facts and circumstances known to management at that time. BTI periodically confirms the accuracy of its estimates with the service providers and makes adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to contract research organizations ("CROs") in connection with clinical studies, amounts paid to contract manufacturing organizations, and fees paid to sites in connection with clinical trials.

The Company bases its expenses related to clinical studies on management's estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trial studies on our behalf. The financial terms of these agreements are subject to an initial negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to vendors exceed the level of services

provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing certain service fees, BTI management estimates the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from management's estimate, management will adjust the accrual or prepaid accordingly. Although the Company does not expect management's estimates to be materially different from amounts actually incurred, management's understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in BTI reporting amounts that are too high or too low in any particular period.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Foreign Exchange Risk

As of December 31, 2022, we had $193,725 of cash and cash equivalents. Our cash and cash equivalents are primarily held in U.S. Government money market funds. We do not participate in any foreign currency hedging activities and have limited exposure to other derivative financial instruments, primarily resulting from the terms and conditions of the OFA Facilities. We did not recognize any significant exchange rate losses during the years ended December 31, 2022 and 2021, respectively.

We do not believe that our cash and cash equivalents have significant risk of default or illiquidity. While we believe our cash and cash equivalents do not contain material market risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash at one or more financial institutions that exceed federally insured limits. In the event of a failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we will be able to access uninsured funds in a timely manner or at all.

Interest Rate Risk

The loans under the Credit Agreement bear interest at a fixed annual rate of 10.25%, payable quarterly, and the RIFA is repaid based on a multiple of invested capital. Consequently, we do not have material interest rate exposure due to our indebtedness.

Capital Market Risk

We currently do not have substantial product revenues and depend on funds raised through other sources. One source of funding includes future debt or equity offerings. Our ability to raise funds in this manner depends upon, among other things, capital market forces affecting our stock price, and on the state of the capital markets generally.

Item 8. Financial Statements and Supplementary Data

The financial statements required pursuant to this item are included in Item 15 of this report and the related report of our independent auditor are presented beginning on page F-1 and are incorporated under this Item by reference. Our independent auditor for the years ended December 31, 2022 and 2021 was Ernst & Young LLP (PCAOB ID: 42), located in Stamford, Connecticut, USA.

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, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and

procedures as of December 31, 2022. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the rules and forms of the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management’s Annual Report on Internal Controls Over Financial Reporting

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in “Internal Control-Integrated Framework (2013)” issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm on internal control over financial reporting due to an exemption established by the JOBS Act for “emerging growth companies.”

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the three months ended December 31, 2022, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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 ABOUT OUR DIRECTORS & EXECUTIVE OFFICERS

The following information with respect to our Board of Directors (the "Board") and executive officers is presented as of March 15, 2023:

Name	Age	Position at BioXcel	Principal Employment
Vimal Mehta, Ph.D.	62	Chief Executive Officer and President, and Director	Same
Richard Steinhart	65	Senior Vice President and Chief Financial Officer	Same
Matthew Wiley	51	Senior Vice President and Chief Commercial Officer	Same
Frank Yocca, Ph.D.	67	Senior Vice President and Chief Scientific Officer	Same
Vincent O'Neill, M.D.	53	Senior Vice President and Chief Medical Officer	Same
Javier Rodriguez	51	Senior Vice President, Chief Legal Officer and Corporate Secretary	Same
Peter Mueller, Ph.D.	66	Chairman of the Board	President at Mueller Health Foundation, a private foundation tackling globally lethal infectious diseases
June Bray	69	Director	Former Senior Vice President, Global Regulatory Affairs and Medical Writing at Allergan, Inc., a pharmaceutical company
Sandeep Laumas, M.D.	54	Director	Chief Business Officer and Chief Financial Officer at Instil Bio, Inc., a pharmaceutical company
Michael Miller	65	Director	Former Executive Vice President, U.S. Commercial at Jazz Pharmaceuticals, Inc., a pharmaceutical company
Krishnan Nandabalan, Ph.D.	60	Director	President and Chief Executive Officer, InveniAI, a company focus on AI applications for drug discovery and development
Michael Votruba, M.D.	57	Director	Director at the Gradus/RSJ Life Sciences Fund, a dedicated fund

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to our annual meeting of stockholders to be held in 2023 (the "2023 Annual Meeting of Stockholders"), which we intend to file with the SEC within 120 days of the year ended December 31, 2022.

Item 11. Executive Compensation

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2022.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2022.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2022.

Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2022.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) Financial Statements:

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits.

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
3.1	Amended and Restated Certificate of Incorporation	10-Q	001-38410	3.1	08/10/2021	
3.2	Amended and Restated Bylaws	8-K	001-38410	3.2	03/13/2018	
4.1	Description of the Registrant's Securities Registered Under Section 12 of the Exchange Act	10-K	001-38410	4.1	03/09/2020	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
4.2	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-222990	4.2	02/26/2018	
4.3	Form of Warrant Agreement under the Credit Agreement and Guaranty, by and among BioXcel Therapeutic, Inc., Oaktree Fund Administration, LLC, the Subsidiary Guarantors from time to time party thereto and the Lenders from time to time party thereto, dated April 9, 2022	8-K	001-38410	4.1	04/19/2022	
4.4	Registration Rights Agreement, dated April 19, 2022, among the Company and Oaktree-TCDRS Strategic Credit, LLC, Oaktree-Forrest Multi-Strategy, LLC, Oaktree-TBMR Strategic Credit Fund C, LLC, Oaktree-TBMR Strategic Credit Fund F, LLC, Oaktree-TBMR Strategic Credit Fund G, LLC, Oaktree-TSE 16 Strategic Credit, LLC, INPRS Strategic Credit Holdings, LLC, Oaktree Strategic Income II, Inc., Oaktree Specialty Lending Corporation, Oaktree Strategic Credit Fund, Oaktree GCP Fund Delaware Holdings, L.P., Oaktree Diversified Income Fund Inc., Oaktree AZ Strategic Lending Fund, L.P., Oaktree Loan Acquisition Fund, L.P., Oaktree LSL Fund Delaware Holdings EURRC, L.P., and Q Boost Holding LLC	8-K	001-38410	4.2	04/19/2022	
10.1+	Second Amended and Restated Separation and Shared Services Agreement, dated March 6, 2020, by and between BioXcel Corporation and BioXcel Therapeutics, Inc.	10-K	001-38410	10.2	03/09/2020	
10.2#	First Amendment to Second Amended and Restated Separation and Shared Services Agreement, dated March 3, 2021, by and between BioXcel LLC and BioXcel Therapeutics Inc.	10-K	001-38410	10.3	03/12/2021	
10.3	Second Amendment to Second Amended and Restated Separation and Shared Services Agreement, dated March 3, 2021, by and between BioXcel LLC and BioXcel Therapeutics Inc.	10-Q	001-38410	10.2	05/09/2022	
10.4#	Amended and Restated Asset Contribution Agreement, effective November 7, 2017,	S-1/A	333-222990	10.2	02/12/2018	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
	by and between BioXcel LLC and BioXcel Therapeutics, Inc.					
10.5	Lease Agreement, dated as of August 20, 2018, by and between Fusco Harbour Associates, LLC, as Landlord, and BioXcel Therapeutics, Inc., as Tenant	8-K	001-38410	10.1	08/23/2018	
10.6	First Amendment, dated August 19, 2020, to Lease Agreement, dated as of August 20, 2018, by and between Fusco Harbour Associates, LLC, as Landlord, and BioXcel Therapeutics, Inc., as Tenant	10-Q	001-38410	10.1	11/12/2020	
10.7@	2017 Equity Incentive Plan	S-1/A	333-222990	10.3	02/12/2018	
10.8@	Form of Incentive Stock Option Agreement under the 2017 Equity Incentive Plan	S-1/A	333-222990	10.4	02/12/2018	
10.9@	Form of Non-Statutory Stock Option Agreement under the 2017 Equity Incentive Plan	S-1/A	333-222990	10.5	02/12/2018	
10.10@	BioXcel Therapeutics, Inc. 2020 Incentive Award Plan and forms of award agreements thereunder	10-Q	001-38410	10.1	08/14/2020	
10.11@	BioXcel Therapeutics, Inc. 2020 Employee Stock Purchase Plan	10-Q	001-38410	10.2	08/14/2020	
10.12@	Form of Indemnification Agreement with directors and executive officers	S-1/A	333-222990	10.6	02/12/2018	
10.13@	Employment Agreement, dated March 7, 2018 by and between BioXcel Therapeutics, Inc. and Vimal Mehta	8-K	001-38410	10.1	03/13/2018	
10.14@	Employment Agreement, dated February 12, 2018, by and between BioXcel Therapeutics, Inc. and Frank Yocca	S-1/A	333-222990	10.11	02/12/2018	
10.15@	Employment Agreement, effective October 2, 2017, by and between BioXcel Therapeutics, Inc. and Richard Steinhart	S-1/A	333-222990	10.12	02/12/2018	
10.16@	Employment Agreement, dated June 1, 2018, by and between BioXcel Therapeutics, Inc. and Dr. Vincent O'Neill, M.D.	8-K	001-38410	10.1	06/07/2018	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
10.17@	Employment Agreement between Javier Rodriguez and BioXcel Therapeutics, Inc., dated February 15, 2021.	10-K	001-38410	10.19	03/12/2021	
10.18@	Employment Agreement between Matthew Wiley and BioXcel Therapeutics, Inc., dated January 12, 2022.	10-K	001-38410	10.20	03/11/2022	
10.19@	Non-Employee Director Compensation Program	10-Q	001-38410	10.4	08/11/2022	
10.20	BioXcel Trademark License Agreement, between the Company and BioXcel LLC	10-Q	001-38410	10.1	05/09/2022	
10.21+&	Credit Agreement and Guaranty, by and among BioXcel Therapeutic, Inc., Oaktree Fund Administration, LLC, the Subsidiary Guarantors from time to time party thereto and the Lenders from time to time party thereto, dated April 19, 2022	10-Q	001-38410	10.1	08/11/2022	
10.22+&	Revenue Interest Financing Agreement, between BioXcel Therapeutics, Inc., Oaktree Fund Administration, LLC and the Purchasers from time to time party thereto, dated April 19, 2022	10-Q	001-38410	10.2	08/11/2022	
10.23+&	Commercial Supply Agreement, between ARx, LLC and BioXcel Therapeutics, Inc., dated April 1, 2022	10-Q	001-38410	10.3	08/11/2022	
10.24	OnkosXcel Therapeutics, LLC and OnkosXcel Employee Holdings, LLC Management Incentive Plan	8-K	001-38410	10.1	08/19/2022	
10.25	Form of Profits Interest Award Agreement under the Management Incentive Plan	8-K	001-38410	10.2	08/19/2022	
21.1	Subsidiaries of BioXcel Therapeutics, Inc.					*
23.1	Consent of Ernst & Young LLP					*
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.					*

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
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.					*
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.					**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
101.INS	Inline eXtensible Business Reporting Language (XBRL) Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					*
101.SCH	Inline XBRL Taxonomy Extension Schema Document					*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					*
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					*

@ Indicates a management contract or any compensatory plan, contract or arrangement.
+ Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.
# Confidential treatment has been granted for portions omitted from this exhibit and those portions have been separately filed with the Securities and Exchange Commission.
& Annexes, schedules, and certain exhibits have been omitted pursuant to Item 601(a)(5)(b)(2) of Regulation S-K. The Registrant hereby agrees to furnish supplementally a copy of any omitted annex, schedule or exhibit to the SEC upon request.
* Filed herewith.
** Furnished herewith.

Item 16. Form 10-K Summary

Not applicable

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

BioXcel Therapeutics, Inc.

Dated: March 15, 2023

By:
/s/ Vimal Mehta
Vimal Mehta, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Dated: March 15, 2023

By:
/s/ Richard Steinhart
Richard Steinhart
Chief Financial Officer
(Principal Financial Officer)

Signature	Title	Date
/s/ Vimal Mehta Vimal Mehta, Ph.D.	Chief Executive Officer and Director *(Principal Executive Officer)*	March 15, 2023
/s/ Richard Steinhart Richard Steinhart	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 15, 2023
/s/ Peter Mueller Peter Mueller, Ph.D.	Chairman of the Board of Directors	March 15, 2023
/s/ June Bray June Bray	Director	March 15, 2023
/s/ Sandeep Laumas Sandeep Laumas, M.D.	Director	March 15, 2023
/s/ Michael Miller Michael Miller	Director	March 15, 2023
/s/ Krishnan Nandabalan Krishnan Nandabalan, Ph.D.	Director	March 15, 2023
/s/ Michal Votruba Michal Votruba	Director	March 15, 2023

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of BioXcel Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of BioXcel Therapeutics, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, changes in stockholders' equity and cash flows for the years then ended, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for the years then ended in conformity with U.S. generally accepted accounting principles.

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/ Ernst & Young LLP

We have served as the Company’s auditor since 2021.

Stamford, Connecticut
March 15, 2023

BIOXCEL THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

(amounts in thousands, except per share amounts)

	December 31, 2022	December 31, 2021
ASSETS		
Current assets		
Cash and cash equivalents	$ 193,725	$ 232,968
Accounts receivable, net	248	—
Inventory	1,985	—
Prepaid expenses	3,067	2,888
Other current assets	3,843	956
Total current assets	$ 202,868	$ 236,812
Property and equipment, net	1,084	1,294
Operating lease right-of-use assets	976	1,247
Other assets	925	86
Total assets	$ 205,853	$ 239,439
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 10,228	$ 4,678
Accrued expenses	18,669	11,492
Due to related parties	422	204
Accrued interest	3,175	—
Other current liabilities	404	293
Total current liabilities	$ 32,898	$ 16,667
Long-term portion of operating lease liabilities	786	1,105
Derivative liabilities	2,343	—
Long-term debt	93,051	—
Total liabilities	$ 129,078	$ 17,772
Commitments and contingencies (Note 17)		
Stockholders' equity		
Preferred stock, $0.001 par value, 10,000 shares authorized; no shares issued and outstanding as of December 31, 2022 and December 31, 2021	$ —	$ —
Common stock, $0.001 par value, 100,000 shares authorized as of December 31, 2022 and December 31, 2021; 28,147 and 27,980 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	28	28
Additional paid-in-capital	488,292	467,427
Accumulated deficit	(411,545)	(245,788)
Total stockholders' equity	$ 76,775	$ 221,667
Total liabilities and stockholders' equity	$ 205,853	$ 239,439

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

BIOXCEL THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

(amounts in thousands, except per share amounts)

	Year ended December 31,	
	2022	2021
Revenues		
Product revenue, net	$ 375	$ —
Operating expenses		
Cost of goods sold	$ 20	$ —
Research and development	91,239	52,708
Selling, general and administrative	68,761	54,227
Total operating expenses	$ 160,020	$ 106,935
Loss from operations	$ (159,645)	$ (106,935)
Other expense (income)		
Interest expense	8,213	40
Interest income	(2,528)	(44)
Other expense, net	427	—
Net loss	$ (165,757)	$ (106,931)
Basic and diluted net loss per share attributable to common stockholders	$ (5.92)	$ (4.05)
Weighted average shares outstanding - basic and diluted	28,015	26,373

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

BIOXCEL THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

(amounts in thousands)

	Common Stock		Additional Paid in Capital	Accumulated Deficit	Total
	Shares	Amount			
Balance as of January 1, 2021	**24,417**	**$ 24**	**$ 345,529**	**$ (138,857)**	**$ 206,696**
Issuance of common shares, net of issuance costs of $3,542	3,279	3	100,990	—	100,993
Stock-based compensation	—	—	19,455	—	19,455
Exercise of stock options	284	1	1,453	—	1,454
Net loss	—	—	—	(106,931)	(106,931)
Balance as of December 31, 2021	**27,980**	**$ 28**	**$ 467,427**	**$ (245,788)**	**$ 221,667**
Issuance of stock purchase warrants	—	—	3,245	—	3,245
Stock-based compensation	—	—	17,337	—	17,337
Exercise of stock options	167	—	283	—	283
Net loss	—	—	—	(165,757)	(165,757)
Balance as of December 31, 2022	**28,147**	**$ 28**	**$ 488,292**	**$ (411,545)**	**$ 76,775**

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

BIOXCEL THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(amounts in thousands)

	Year ended December 31, 2022	2021
OPERATING CASH FLOW ACTIVITIES:		
Net loss	$ (165,757)	$ (106,931)
Reconciliation of net loss to net cash used in operating activities		
Depreciation	327	297
Accretion of debt discount and amortization of financing costs	860	—
Change in fair value of derivative liabilities	389	—
Stock-based compensation expense	17,337	19,455
Payable-in-kind interest on Credit Agreement	807	—
Loss on disposal of equipment	22	46
Changes in operating assets and liabilities		
Accounts receivable	(248)	—
Inventory	(1,985)	—
Prepaid expenses, other current assets and other assets	(3,905)	103
Operating lease right-of-use assets	271	264
Accounts payable, accrued expenses, and other current liabilities	13,030	4,850
Accrued interest	3,804	—
Operating lease liabilities	(293)	(237)
Net cash used in operating activities	$ (135,341)	$ (82,153)
INVESTING CASH FLOW ACTIVITIES:		
Purchases of property and equipment	$ (139)	$ (445)
Net cash used in investing activities	$ (139)	$ (445)
FINANCING CASH FLOW ACTIVITIES:		
Proceeds from long-term debt	$ 98,600	$ —
Debt issuance costs	(2,646)	—
Proceeds from issuance of common stock, net of issuance costs	—	100,993
Exercise of stock options	283	1,454
Net cash provided by financing activities	$ 96,237	$ 102,447
Net (decrease) increase in cash and cash equivalents	$ (39,243)	$ 19,849
Cash and cash equivalents, beginning of the period	232,968	213,119
Cash and cash equivalents, end of the period	$ 193,725	$ 232,968
Supplemental cash flow information:		
Issuance of stock purchase warrants	$ 3,245	$ —
Interest paid	$ 2,697	$ 40
Purchases of property and equipment in accounts payable and accrued expenses	$ —	$ 22

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

BIOXCEL THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(amounts in thousands, except per share amounts and where otherwise noted)

Note 1. Nature of the Business

BioXcel Therapeutics, Inc. ("BTI" or the "Company") is a biopharmaceutical company utilizing artificial intelligence ("AI") approaches to develop transformative medicines in neuroscience and immuno-oncology. The Company is focused on utilizing cutting-edge technology and innovative research to develop high-value therapeutics aimed at transforming patients' lives. BTI employs a unique AI platform to reduce therapeutic development costs and potentially accelerate timelines. The Company's approach leverages existing approved drugs and/or clinically evaluated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indices. BTI management believes this differentiated approach has the potential to reduce the expense and time associated with drug development in diseases with substantial unmet medical needs.

As used in these consolidated financial statements, unless otherwise specified or the context otherwise requires, the terms "BioXcel LLC" refers to the Company's former parent and current significant stockholder, BioXcel LLC and, its predecessor, BioXcel Corporation. "OnkosXcel" refers to BTI's wholly owned subsidiary for its advanced immuno-oncology assets, OnkosXcel Therapeutics, LLC.

On April 6, 2022, BTI announced that the United States ("U.S.") Food and Drug Administration ("FDA") approved IGALMI (dexmedetomidine or "Dex") sublingual film for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults. IGALMI is approved to be self-administrated by patients under the supervision of a health care provider. The Company deployed the first phase of its sales team for high priority targets in May 2022. Furthermore, on July 6, 2022, BTI announced that IGALMI, was commercially available in doses of 120 and 180 microgram through the Company's third-party logistics provider and was available for order through wholesalers.

The Company's most advanced clinical development program is BXCL501, an investigational proprietary, orally dissolving, film formulation of Dex for the treatment of agitation associated with psychiatric and neurological disorders.

BTI continues to conduct clinical trials evaluating BXCL501 for the acute treatment of agitation in Alzheimer's disease patients, and for adjunctive treatment of patients with Major Depressive Disorder ("MDD"). The Company is also planning clinical trials for the at-home use of BXCL501 for agitation associated with bipolar disorders and schizophrenia.

The Company's advanced immuno-oncology asset, BXCL701, is an investigational, orally administered systemic innate immune activator for the treatment of a rare form of prostate cancer and advanced solid tumors that are refractory or treatment naïve to checkpoint inhibitors.

BTI was incorporated under the laws of the State of Delaware on March 29, 2017. The Company's principal office is in New Haven, Connecticut.

Impact of COVID-19 Pandemic

The COVID-19 pandemic and responsive measures have significantly impacted, both directly and indirectly, businesses and commerce.

The Company continues to work closely with clinical sites to monitor the potential impact of the evolving COVID-19 pandemic and the spread of its variants. To date, BTI has not experienced any significant delays in any of its ongoing or planned clinical trials, except for occasional COVID-19 related disruptions, such as to its TRANQUILITY II trial. However, this could change rapidly.

Note 2. Basis of Presentation

The accompanying consolidated financial statements include those of the Company and its subsidiaries after elimination of all intercompany accounts and transactions and have been prepared in conformity with United States ("U.S.") Generally Accepted Accounting Principles ("GAAP").

The Company believes that its existing cash and cash equivalents will be sufficient to cover its cash flow requirements for at least the next twelve months from the issuance of these financial statements. However, the Company's future requirements may change and will depend on numerous factors.

Note 3. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in accordance with U.S. GAAP requires management to make estimates and assumptions that affect amounts reported in the consolidated financial statements and notes thereto. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may ultimately materially differ from these estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. As of December 31, 2022 and 2021, cash equivalents were comprised primarily of money market funds. Cash and cash equivalents held at financial institutions may at times exceed federally insured amounts. BTI management believes it mitigates such risk by investing in or through major financial institutions.

Accounts Receivable, Net

Accounts receivable arise from sales of IGALMI and represent amounts due from distributors. Payment terms generally range from 30 to 75 days from the date of the sale transaction, and accordingly, do not involve a significant financing component. Receivables from product sales are recorded net of allowances which generally include distribution fees, prompt payment discounts, chargebacks, and credit losses. Allowances for distribution fees, prompt payment discounts and chargebacks are based on contractual terms. The Company estimated the current expected credit losses of its accounts receivable by assessing the risk of loss and available relevant information about collectability, existing contractual payment terms, actual payment patterns of its customers, individual customer circumstances, and reasonable and supportable forecast of economic conditions expected to exist throughout the contractual life of the receivable. Based on its assessment, as of December 31, 2022, the Company determined that an allowance for credit losses was not required.

Concentrations of Credit Risk

The Company sells IGALMI through a drop-ship program under which orders from hospitals and similar health care institutions are processed through wholesalers, but shipments of the product are sent directly to the individual hospitals and similar health care institutions. BTI also contracts directly with intermediaries such as group purchasing organizations ("GPOs"). All trade accounts receivables are due from the distributor that fulfills orders on behalf of the Company.

Inventory

Inventory is stated at the lower of cost or net realizable value. Cost of inventory is determined on a first-in, first-out basis.

BTI capitalizes inventory costs associated with the Company's products prior to regulatory approval, when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development expense in the Consolidated Statements of Operations.

The Company performs an assessment of the recoverability of capitalized inventory during each reporting period and writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, will be recorded within cost of goods sold in the Consolidated Statements of Operations. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected, write-downs of inventory may be required.

Property and Equipment

Property and equipment are recorded at cost and depreciated over the shorter of their remaining lease term or their estimated useful life on a straight-line basis as follows:

Equipment	3-5 years
Furniture	7 years
Leasehold improvements	Lesser of life of improvement or lease term

Expenditures for maintenance and repairs which do not improve or extend the useful lives of the respective assets are expensed as incurred. When assets are sold or retired, the related cost and accumulated depreciation are removed from their respective accounts and any resulting gain or loss is included within selling, general and administrative expenses in the Consolidated Statements of Operations.

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 undiscounted future net cash flows expected to be generated from its use and disposition. Impairment charges are recognized at the amount by which the carrying amount of an asset exceeds the fair value of the asset. Assets to be disposed of are reported at the lower of the carrying amount or the fair value less costs to sell.

Leases

The Company determines if an arrangement is a lease at inception. Operating leases are included in operating lease right-of-use (“ROU”) assets, other current liabilities, and the long-term portion of operating lease liabilities in the Consolidated Balance Sheets.

ROU assets represent BTI’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 lease liabilities are recognized at commencement date based on the present value of lease payments over the lease term. The Company uses the implicit rate when readily determinable. As BTI’s leases do not provide an implicit rate, it used an incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. The operating lease ROU asset also includes any prepaid lease payments made and excludes lease incentives. The Company’s leases may include options to extend the lease; such options are included in determining the lease term when it is reasonably certain that BTI will exercise that option. Lease expense is recognized on a straight-line basis over the lease term.

Debt and Detachable Warrants

Detachable warrants are evaluated for classification as either equity instruments, derivative liabilities, or liabilities depending on the specific terms of the warrant agreement. In circumstances in which debt is issued with equity-classified warrants, the proceeds from the issuance of debt are first allocated to the debt and the warrants at their estimated fair values. The portion of the proceeds allocated to the warrants are accounted for as paid-in capital and a debt discount. The remaining proceeds, as further reduced by discounts created by the bifurcation of any embedded derivatives, are allocated to the debt. Detachable warrants classified as derivative liabilities are accounted for as indicated under “*Derivative Assets and Liabilities*” section of this Note and as a debt discount. The Company accounts for debt as liabilities measured at amortized cost and amortizes the resulting debt discount from the allocation of proceeds to interest expense using the effective interest method over the expected term of the debt instrument. The Company considers

whether there are any embedded features in debt instruments that require bifurcation and separately accounts for them as derivative financial instruments.

The Company entered into financing arrangements, the terms of which involve significant assumptions and estimates, including future net product sales, in determining interest expense, amortization period of the debt discount, as well as the classification between current and long-term portions. In estimating future net product sales, the Company assesses prevailing market conditions using various external market data against the Company's anticipated sales and planned commercial activities. Consequently, the Company imputes interest on the carrying value of the debt and records interest expense using an imputed effective interest rate. The Company reassesses the expected payments during each reporting period and accounts for any changes through an adjustment to the effective interest rate on a prospective basis, with a corresponding impact to the classification of the Company's current and long-term portions of the debt.

Derivative Assets and Liabilities

Derivative assets and liabilities are recorded on the Company`s Consolidated Balance Sheets at their fair value on the date of issuance and are revalued on each balance sheet date until such instruments are settled or expire, with changes in the fair value between reporting periods recorded as other income or expense within other expense, net in the Consolidated Statements of Operations.

The Company does not use derivative instruments for speculative purposes or to hedge exposures to cash-flow or market risks. Certain financing facilities entered into by the Company include freestanding financial instruments and/or embedded features that require separate accounting as derivative assets and/or liabilities.

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.

Revenue Recognition

The Company's revenues consist of product sales of IGALMI.

BTI recognizes revenue when its customers obtain control of promised goods or services, in an amount that reflects the consideration that the Company expects to receive in exchange for those goods or services. To determine revenue recognition, BTI management performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

The Company assesses whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such goods and services are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and (ii) the Company's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

The Company allocates the transaction price (the amount of consideration it expects to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which the Company expects to be entitled.

BTI distributes IGALMI in the U.S. through arrangements with a distributor, wholesalers, and GPOs. The distributor and wholesalers help process and fulfill orders from hospitals on the Company's behalf. The Company believes the hospitals are its customers.

The Company recognizes product revenues, net of consideration payable to customers, as well as variable consideration related to certain allowances and accruals that are determined using either the expected value or most likely amount method, depending on the type of the variable consideration, in its consolidated financial statements at the point in time when control transfers to the customer, which is typically when the product has been delivered to the customer's location. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. The Company's only performance obligation identified for IGALMI is to deliver the quantity of product ordered to the location specified by the customer's order. The Company records shipping and handling costs associated with delivery of product to its customers within selling, general and administrative expenses on its Consolidated Statements of Operations. Under the Company's current product sales arrangements, BTI does not have contract assets (unbilled receivables), as it generally invoices its customer at the time of revenue recognition, and contract liabilities, as the Company generally does not receive prepayments from its customers prior to product delivery.

BTI sells IGALMI at wholesale acquisition cost and calculates product revenue net of variable consideration and consideration payable to third parties associated with distribution of product. The Company records reserves, based on contractual terms, for the following components of consideration related to product sold during the reporting period. Calculating these amounts involves estimates and judgments, and the Company reviews these estimates quarterly and records any material adjustments in the period they are identified, which affects net product revenue and earnings in the period such variances occur.

Trade Discounts and Allowances

The Company provides the distributor and wholesalers with discounts for prompt payment and pays fees to the distributor, wholesalers and GPOs related to distribution of the product. BTI expects the relevant third parties to earn these discounts and fees, and therefore it deducts such amounts from gross product revenue and accounts receivable at the time it recognizes the related revenue.

Government Rebates

IGALMI is eligible for purchase by, or qualifies for reimbursement from, Medicaid and other U.S. government programs that are eligible for rebates on the price they pay for the product. To determine the appropriate amount to reserve for these rebates, BTI applies the applicable government discount to these sales, and estimates the portion of total rebates that it anticipates will be claimed. The Company deducts certain government rebates from gross product revenue and accounts receivable at the time it recognizes the related revenue; other government rebates are recognized as an accrued liability at the time BTI recognizes the related revenue.

Chargebacks

BTI provides product discounts to hospitals associated with certain GPOs. The Company estimates the chargebacks that it expects to be obligated to provide based upon the terms of the applicable arrangements. BTI deducts such amounts from gross product revenue and accounts receivable at the time it recognizes the related revenue.

Product Returns

The Company provides contractual return rights to its customers including the right to return product within six months of product expiration and up to 12 months after product expiration, as well as for incorrect shipments, and damaged or defective product, which the Company expects to be rare. Management expects product returns to be minimal, thus BTI recognizes a nominal allowance for product returns at the time of each sale. In the future, if any of these factors and/or the history of product returns changes, the Company will adjust the allowance for product returns.

BTI classifies all fees paid to the distributor, other than those discussed above and those related to warehouse operations, as selling, general and administrative expenses on its Consolidated Statements of Operations. Fees paid to the distributor for warehouse operations are classified as costs of goods sold on BTI's Consolidated Statements of Operations.

Cost of Goods Sold

Cost of goods sold includes the cost of producing and distributing inventories that are related to product revenues during the respective period. Cost of goods sold may also include costs related to excess or obsolete inventory adjustment charges, as well as costs related to warehouse operations paid to distributors.

Stock-Based Compensation

The Company measures and recognizes stock-based compensation expense based on estimated fair value for all share-based awards made to employees, non-employee service providers, and directors, including stock options and restricted stock units ("RSUs"). The Company's 2017 Equity Incentive Plan (the "2017 Plan") became effective in August 2017. The Company's 2020 Incentive Award Plan (the "2020 Plan") became effective in May 2020. Following the effective date of the 2020 Plan, the Company ceased granting awards under the 2017 Plan; however, the terms and conditions of the 2017 Plan continue to govern any outstanding awards granted thereunder.

The Company's stock-based awards are valued at fair value on the date of grant and that fair value is recognized as an expense in the Consolidated Statements of Operations over the requisite service period using the accelerated attribution method. The estimated fair value of stock-based awards was determined using the Black-Scholes pricing model on the date of grant.

The Black-Scholes pricing model is affected by the Company's stock price, as well as assumptions regarding variables including, but not limited to, the strike price of the instrument, the risk-free rate, the expected stock price volatility over the term of the awards, and expected term of the award. The Company has elected to account for forfeitures as they occur, by reversing compensation cost when the award is forfeited.

Research and Development Costs

Research and development expenses include wages, benefits, non-cash stock-based compensation, facilities, supplies, external services, clinical study, manufacturing costs related to clinical trials and other expenses that are directly related to the Company's research and development activities. At the end of the reporting period, the Company compares payments made to third-party service providers to the estimated progress toward completion of the research or development objectives. Depending on the timing of payments to the service providers and the progress that the Company estimates has been made for the program as a result of the level of service provided, the Company may record net prepaid or accrued expense relating to these costs. Such estimates are subject to change as additional information becomes available. The Company expenses research and development costs as incurred.

The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary.

Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period.

Patent Costs

Costs related to filing and pursuing patent applications are recorded in selling, general and administrative expenses and are expensed as incurred since recoverability of such expenditures is uncertain.

Fair Value of Financial Instruments

The Company measures certain financial assets and liabilities at fair value, which is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The Company applies a fair value hierarchy that distinguishes between (1) market participant assumptions developed based on market data obtained from independent sources, or observable inputs, and (2) an

entity's own assumptions about market participant assumptions developed based on the best information available in the circumstances, or unobservable inputs. The fair value hierarchy consists of three broad levels, which gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1) and the lowest priority to unobservable inputs (Level 3). Fair value measurements must be classified and disclosed in one of the following three categories:

- Level 1: Quoted prices (unadjusted) in active markets that are accessible at the measurement date for assets or liabilities. The fair value hierarchy gives the highest priority to Level 1 inputs.
- Level 2: Directly or indirectly observable inputs as of the reporting date through correlation with market data, including quoted prices for similar assets and liabilities in active markets and quoted prices in markets that are not active. Level 2 also includes assets and liabilities that are valued using models or other pricing methodologies that do not require significant judgment since the input assumptions used in the models, such as interest rates and volatility factors, are corroborated by readily observable data from actively quoted markets for substantially the full term of the financial instrument.
- Level 3: Unobservable inputs that are supported by little or no market activity and reflect the use of significant management judgment. These values are generally determined using pricing models for which the assumptions utilize management's estimates of market participant assumptions.

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 considering counterparty credit risk in its assessment of fair value.

Income Taxes

BTI uses an asset and liability approach for financial accounting and reporting of income taxes. Deferred tax assets and liabilities are determined based on temporary differences between financial reporting and tax basis assets and liabilities and are measured by applying enacted rates and laws to taxable years in which differences are expected to be recovered or settled. Further, the effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that the rate changes. A valuation allowance is required when it is "more likely than not" that all or a portion of deferred tax assets will not be realized.

U.S. GAAP prescribes a comprehensive model for how a company should recognize, measure, present and disclose in its financial statements uncertain tax positions that the Company has taken or expects to take on a tax return, including a decision whether to file or not file a return in a particular jurisdiction. The Company's financial statements reflect expected future tax consequences of such positions presuming the taxing authorities' full knowledge of the position and all relevant facts.

The Company does not have any unrecognized tax benefits as of December 31, 2022 and 2021. BTI reviews all tax positions to ensure the tax treatment selected is sustainable based on its technical merits and that the position would be sustained if challenged.

Earnings (Loss) per Share

Earnings (loss) per share ("EPS") is calculated by dividing net income or loss attributable to common stockholders by the weighted average number of shares of common stock that were outstanding. Diluted EPS is calculated by adjusting the weighted average number of shares of common stock that were outstanding for the dilutive effect of common stock equivalents. In periods in which a net loss is recorded, no effect is given to potentially dilutive securities, since the effect would be antidilutive.

Segment Information

The Company operates in a single segment. Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making

decisions regarding resource allocation and assessing performance. To date, the Company's chief operating decision maker has made such decisions and assessed performance at the Company level as one segment.

Recent Accounting Pronouncements

Recently adopted accounting pronouncements

In December 2019, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU No. 2019-12"), which amends the existing guidance relating to the accounting for income taxes. ASU No. 2019-12 is intended to simplify the accounting for income taxes by removing certain exceptions to the general principles of accounting for income taxes and to improve the consistent application of U.S. GAAP for other areas of accounting for income taxes by clarifying and amending existing guidance. ASU No. 2019-12 was effective for interim and annual periods beginning after December 15, 2020. The adoption of ASU No. 2019-12 on January 1, 2021 did not have a material impact on the Company's consolidated financial statements.

Accounting Pronouncements effective in future periods

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, and subsequent amendments to the initial guidance (collectively, "Topic 326"). Topic 326 requires measurement and recognition of expected credit losses for financial assets held. Topic 326 was to be effective for reporting periods beginning after December 15, 2019, with early adoption permitted. In November 2019, the FASB issued ASU No. 2019-10, *Financial Instruments - Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842) - Effective Dates*, which deferred the effective dates of Topic 326 for the Company, until fiscal year 2023. The Company does not expect the adoption of Topic 326 to have a material impact on its consolidated financial statements**.**

Note 4. Inventory

Inventory consists of the following:

	December 31, 2022
Raw materials	$ 682
Work-in-process	708
Finished goods	595
Total inventory	$ 1,985

There were no write-downs of inventory for the year ended December 31, 2022. The Company did not have commercial inventory as of December 31, 2021.

Note 5. Property and Equipment, net

Property and Equipment, net consists of the following:

	December 31, 2022	December 31, 2021
Computers and equipment	$ 213	$ 167
Furniture	575	572
Leasehold improvements	1,181	1,133
Construction-in-process	—	24
Total property and equipment	$ 1,969	$ 1,896
Accumulated depreciation	(885)	(602)
Total property and equipment, net	$ 1,084	$ 1,294

Depreciation expense was $327 and $297 for the years ended December 31, 2022 and 2021, respectively.

Note 6. Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2022	December 31, 2021
Accrued research and development expenses	$ 8,659	$ 5,762
Accrued compensation and benefits	6,370	3,968
Accrued professional expenses	2,738	1,324
Accrued taxes	82	302
Other accrued expenses	820	136
Total accrued expenses	$ 18,669	$ 11,492

Note 7. Transactions with BioXcel LLC

The Company entered into a Separation and Shared Services Agreement with BioXcel LLC that took effect on June 30, 2017, as amended and restated thereafter (the “Services Agreement”), pursuant to which services provided by BioXcel LLC, through its subsidiaries in India and the U.S., will continue indefinitely, as agreed upon by the parties. These services are primarily for drug discovery, CMC and administrative support.

Service charges recorded under the Services Agreement for the years December 31, 2022 and 2021 were as follows:

	Year ended December 31,	
	2022	2021
Research and development	$ 1,151	$ 1,184
Selling, general and administrative	250	218
Total	$ 1,401	$ 1,402

As of December 31, 2022 and 2021, $310 and $204, respectively, of these service charges are included in due to related parties in the Company's Consolidated Balance Sheets.

Note 8. Debt and Credit Facilities

Debt, net of unamortized discounts and financing costs, consists of the following:

	December 31, 2022
Revenue Interest Financing Agreement ("RIFA")	$ 30,000
RIFA accrued interest	2,041
RIFA payments	(10)
RIFA debt liability	$ 32,031
Estimated portion of RIFA debt liability to be paid within one-year	(1,401)
RIFA long-term debt liability	$ 30,630
Credit Agreement and Guaranty	70,000
Payable-in-kind interest on Credit Agreement and Guaranty	807
Total long-term debt liability	$ 101,437
Unamortized debt discounts and issuance costs	(8,386)
Total long-term debt	$ 93,051

On April 19, 2022 (the "Effective Date"), the Company entered into two strategic financing agreements: (i) a Credit Agreement and Guaranty (the "Credit Agreement") by and among the Company, as the borrower, certain subsidiaries of the Company from time to time party thereto as subsidiary guarantors, the lenders party thereto (the "Lenders"), and Oaktree Fund Administration LLC ("OFA") as administrative agent, and (ii) a Revenue Interest Financing Agreement (the "RIFA"; and together with the Credit Agreement, the "OFA Facilities") by and among the Company, the purchasers party thereto (the "Purchasers") and OFA as administrative agent. Under the OFA Facilities, the Lenders and the Purchasers agreed to, in the aggregate between the two OFA Facilities, provide up to $260,000 in gross funding to support the Company's commercial activities of IGALMI sublingual film. In addition, the OFA Facilities are intended to support the expansion of clinical development efforts of BXCL501, which includes a Phase 3 program for the acute treatment of agitation in patients with Alzheimer's disease, and for general corporate purposes. The Lenders and Purchasers are comprised of affiliates of Oaktree Capital Management, L.P. and Qatar Investment Authority.

A summary of the OFA Facilities is provided below.

Credit Agreement

The Credit Agreement provides up to $135,000 in senior secured term loans, of which the initial Tranche A of $70,000 was funded on April 28, 2022, and the remaining tranches may be borrowed at the Company's option prior to December 31, 2024, subject to satisfaction of certain conditions, including regulatory and financial milestones. Tranche B of the Credit Agreement is $35,000 and is available upon satisfaction of certain conditions, including receipt of certain regulatory and financial milestones. Tranche C of the Credit Agreement is $30,000 and is available upon satisfaction of

certain conditions, including specified minimum net sales of the Company attributable to sales of BXCL501 for a trailing twelve consecutive month period. As of December 31, 2022, $65,000 remained available under the Credit Agreement, subject to achievement of the specified conditions and milestones.

The loans under the Credit Agreement do not amortize and mature on the fifth anniversary of the Effective Date; provided that the Company may, at its option, extend the maturity date to the sixth anniversary if, prior to December 31, 2024, the Company receives and satisfies certain conditions including receipt of certain regulatory and financial milestones. Borrowings under the Credit Agreement are issued at a 200-basis point original issue discount and bear interest at a fixed annual rate of 10.25%, payable quarterly. Of such interest, 225-basis points per annum is, at the Company's option, payable in kind by capitalizing and adding such interest to the outstanding principal amount of loans from the first payment date on which such interest is owed through, and including, the third anniversary of such payment date, unless, with respect to any payment date, the Company elects to pay all or a portion of such interest in cash. The Company is required to pay a ticking fee equal to 0.75% per annum on the undrawn amount of the commitments, payable quarterly commencing 120 days after the funding of the Tranche A term loan through the termination of the commitments, which is expensed as incurred and recognized as interest expense in the Consolidated Statements of Operations. The Company may voluntarily prepay the Credit Agreement at any time subject to a prepayment fee.

The Company's obligations under the Credit Agreement are guaranteed by BTI's existing and subsequently acquired or organized subsidiaries, subject to certain exceptions. BTI's obligations under the Credit Agreement and the related guarantees thereunder are secured, subject to customary permitted liens and other agreed upon exceptions, by (i) a pledge of all of the equity interests of all of the Company's existing and any future direct subsidiaries, and (ii) a perfected security interest in all of its and the guarantors' tangible and intangible assets (except that the guarantees provided by the BXCL701 Subsidiaries (as defined below) are unsecured).

The Credit Agreement contains customary representations and warranties and customary affirmative and negative covenants, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of other indebtedness, and dividends and other distributions, subject to certain exceptions, including specific exceptions with respect to product commercialization and development activities. The Company must also comply with certain financial covenants, including (i) maintenance of cash or permitted cash equivalent investments in accounts controlled by OFA for the Lenders, of at least (a) $15,000 from the Effective Date until the date on which the second tranche of loans are funded (the "Step-Up Date") and (b) $20,000 from and after the Step-Up Date, provided, in the case of (a) and (b), that following any Permitted BXCL701 Release Event (as defined below), such amount will increase by $12,500, and following such time as unaffiliated third parties hold ownership of at least 30% of the equity interests in the BXCL701 Subsidiaries (as defined below), such amount will increase by an additional $5,000 (provided, that such amount will in no event exceed 50% of the aggregate amount of loans outstanding at any time); and (ii) a minimum revenue test, measured quarterly beginning with the Company's fiscal quarter ending on December 31, 2023 (such six-month period the "Revenue Covenant Measurement Period"), that requires it and its subsidiaries' consolidated net revenue for the six consecutive month period ending on the last day of each such fiscal quarter to not be less than a minimum revenue amount specified in the Credit Agreement (such testing date, the "Revenue Covenant Measurement Testing Date" and the covenant described in this clause (ii) the "Revenue Covenant"). The Company's failure to comply with the financial covenants will result in an event of default, subject to certain cure rights with respect to the Revenue Covenant. With respect to the Revenue Covenant, the Company would be required to pay the Lenders an amount in respect of the Revenue Covenant, and any such payment will be applied to the prepayment of the loans under the Credit Agreement.

Notwithstanding the foregoing, the Credit Agreement permits OnkosXcel (together with OnkosXcel Employee Holdings, LLC ("Employee Holdings"), a subsidiary of BTI, and their respective subsidiaries, the "BXCL701 Subsidiaries") to receive third-party investment or transfer all or substantially all of their assets to an unaffiliated third-party, in each case subject to terms and conditions set forth in the Credit Agreement, including the escrow of certain proceeds received by BTI and its subsidiaries (other than the BXCL701 Subsidiaries) in respect of these disposition events and, under circumstances set forth in the Credit Agreement, the mandatory prepayment of such escrowed amounts. The Company's equity interests in the BXCL701 Subsidiaries have been pledged in support of its obligations under the Credit Agreement, and the BXCL701 Subsidiaries have provided direct guarantees of BTI's obligations under the Credit Agreement on an unsecured basis. However, the pledge, guarantee and other obligations of the BXCL701 Subsidiaries under the Credit Agreement will be released upon certain agreed upon events ("Permitted BXCL701

Release Events"), including an initial public offering by the BXCL701 Subsidiaries or the ownership by unaffiliated third parties of at least 20% of the equity interests in the BXCL701 Subsidiaries.

The Credit Agreement contains events of default that are customary for financings of this type relating to, among other things, payment defaults, breach of covenants, breach of representations and warranties, cross default to material indebtedness, bankruptcy-related defaults, judgment defaults, breach of the financial covenants described above, and the occurrence of certain change of control events. In certain circumstances, events of default are subject to customary cure periods. Following an event of default and any applicable cure period, the Lenders will have the right upon notice to terminate any undrawn commitments and may accelerate all amounts outstanding under the Credit Agreement, in addition to other remedies available to them as the Company's secured creditors.

Revenue Interest Financing Agreement

The RIFA provides up to $120,000 in financing in exchange for a capped revenue interest on net sales of IGALMI, and other future BXCL501 products, if any, that receive regulatory approval for sale. The initial Tranche A of $30,000 was funded on July 8, 2022, and the remaining tranches may be borrowed at the Company's option prior to December 31, 2024, subject to satisfaction of certain conditions, including certain regulatory, patent, and financial milestones. The effective interest rate on the RIFA as of December 31, 2022, was approximately 14%.

Under the terms of the RIFA, the Purchasers will receive tiered revenue interest payments on U.S. net sales of IGALMI, and other future BXCL501 products, if any, that receive regulatory approval for sale, equal to a royalty ranging from 0.375% to 7.750% of net sales of IGALMI, and other future BXCL501 products, if any, approved for sale in the U.S., subject to a hard cap equal to 1.75x the total amount funded. In addition, if the conditions to the second tranche of the financing provided under the RIFA have been met, once payments equal to the hard cap have been received by the Purchasers, the Company will be required to make revenue interest payments equal to a flat 0.375% royalty on U.S. net sales of IGALMI, and other future BXCL501 products, if any, that receive regulatory approval for sale, through and including March 31, 2036 (the "Tail Royalty"). The Company is also required to make certain additional payments to the Purchasers from time to time to ensure that the aggregate amount of payments received by the Purchasers under the RIFA are at least equal to certain agreed upon minimum levels as of certain specified dates, subject to terms and conditions set forth in the RIFA. Revenue interest payments due under the RIFA are payable quarterly based on net sales.

Any time after the initial funding of the RIFA, BTI has the right (the "BTI Call Option"), but not the obligation, to buy out the Purchasers' interests in the revenue interest payments at an agreed upon repurchase price. The BTI Call Option can be exercised in year one, two, three and thereafter at a multiple of the Purchasers invested capital of 1.225x,1.375x, 1.525x and 2.25x, respectively. The Purchasers will not be entitled to any Tail Royalty if the BTI Call Option is exercised before the third anniversary of the Effective Date.

The Company's obligations under the RIFA are secured, subject to customary permitted liens and other agreed upon exceptions and subject to an intercreditor agreement between OFA for the Credit Agreement and RIFA, by a perfected security interest in (i) accounts receivable arising from net sales of BXCL501 products in the U.S. and one or more segregated bank accounts maintained for the purpose of receiving payments in respect of such accounts receivable, (ii) intellectual property that is claiming or covering BXCL501 itself or any method of using, making or manufacturing BXCL501 and (iii) regulatory approvals, clinical data, and all other assets that underlie BXCL501.

The RIFA contains customary representations and warranties and certain restrictions on the Company's ability to incur indebtedness and grant liens on intellectual property related to BXCL501. In addition, the RIFA provides that if certain events occur, including certain bankruptcy events, failure to make payments, a change of control, an out-license or sale of all of the rights in and to BXCL501 in the U.S., in each case except a permitted licensing transaction (as defined in the RIFA) and, subject to applicable cure periods, material breach of the covenants in the RIFA, OFA, at the direction of the Purchasers, may require the Company to repurchase the Purchasers' interests in the revenue interest payments at an agreed upon repurchase price.

Tranche B and C of the RIFA are each $45,000 and are available upon satisfaction of certain conditions, including receipt of certain regulatory and patent related milestones and specified minimum net sales of BXCL501 during any

consecutive twelve-month period. As of December 31, 2022, $90,000 remained available under the RIFA, subject to achievement of the specified conditions and milestones.

Warrants and Equity Investment Right

In connection with the Credit Agreement, on the Effective Date, the Company granted warrants to the Lenders to purchase up to 278 shares of its common stock (the "BTI Warrants") at an exercise price of $20.04 per share. The BTI Warrants will expire on April 19, 2029, are freely transferable and may be net exercised at the holder's election. In addition, pursuant to the Credit Agreement, the Lenders have the right to purchase shares of the Company's common stock after the Effective Date, so long as borrowings under the Credit Agreement are outstanding, for a purchase price of $5,000 at a price per share equal to a 10% premium to the volume-weighted average price of the common stock over the 30 trading days prior to the Lenders' election to proceed with such equity investment (the "Equity Investment Right"). BTI entered into a registration rights agreement with the Lenders and filed a registration statement on Form S-3 to register the shares issuable upon exercise of the BTI Warrants and, if issued, the shares related to the Equity Investment Right, for resale. The maximum shares of BTI common stock issuable under the BTI Warrants and Lenders' Equity Investment Right is 5,593.

As part of the Credit Agreement, OnkosXcel, a wholly owned subsidiary of BTI, granted warrants to the Lenders to purchase 175 individual limited liability company units (which number of units is not in thousands; referred to herein as the "OnkosXcel Warrants"). The strike price of the OnkosXcel Warrants is formulaic based on the value of OnkosXcel at the time of exercise and can only be exercised upon occurrence of an equity related liquidity event for OnkosXcel of at least $20,000. The exercise price per unit of the OnkosXcel Warrants will be set upon the earlier of the closing of the next sale (or series of related sales) by OnkosXcel of equity securities of OnkosXcel with aggregate proceeds of not less than $20,000 to unrelated third parties (the "Next Equity Financing") at an exercise price per unit equal to a 10% premium over the price per unit of the equity securities sold by OnkosXcel in such Next Equity Financing or, in the event of a sale of OnkosXcel prior to the Next Equity Financing or an initial public offering constituting the Next Equity Financing, the lesser of (x) 75% of the fair value of the consideration to be paid for a unit upon the consummation of such transaction and (y) 150% of the valuation applicable to the initial profits units issued by OnkosXcel after the closing of the Credit Agreement. The OnkosXcel Warrants are transferable with approval from BTI, which cannot be unreasonably withheld, expire on April 19, 2029, and may be net exercised at the holder's election.

Maturities of long-term debt are expected to be as follows:

	December 31, 2022
2023	$ —
2024	$ —
2025	$ 137
2026	$ 10,479
2027	$ 85,707
Thereafter	$ 5,114

Interest expense was as follows:

	Year ended December 31,	
	2022	2021
Interest expense	$ 7,353	$ 40
Accretion of debt discount and amortization of financing costs	860	—
Total interest expense	$ 8,213	$ 40

Note 9. Derivative Financial Instruments

BTI identified certain freestanding financial instruments and/or embedded features that require separate accounting from the borrowings under the OFA Facilities. This includes the OnkosXcel Warrants and Equity Investment Right held by the Lenders, along with certain put/call options. The OnkosXcel Warrants and Equity Investment Right do not meet certain scope exceptions under U.S. GAAP, primarily because the exercise prices and number of shares of the Company's common stock issuable under the instruments are variable, and the instruments meet the definition of a derivative instrument. Therefore, these instruments are recorded as derivative liabilities in the Consolidated Balance Sheets. The respective derivative liabilities are recorded at fair value on the date of issuance and are revalued on each balance sheet date until such instruments are settled or expire, with changes in the fair value between reporting periods recorded within other expense, net in the Company's Consolidated Statements of Operations.

Note 10. Common Stock Financing Activities

In June 2021, the Company sold, in a registered offering, 3,155 shares of its common stock at a public offering price of $31.70 per share. The Company received proceeds of $96,937, net of issuance costs of $3,042.

In May 2021, the Company entered into an Open Market Sale Agreement (the "Sale Agreement") with Jefferies LLC ("Jefferies") pursuant to which the Company could offer and sell shares of its common stock, having an aggregate offering price of up to $100,000, from time to time, through an "at the market offering" program under which Jefferies will act as sale agent. The Company sold 124 shares under the Sale Agreement in June 2021. As of December 31, 2021, the Company received proceeds of $4,056, net of issuance costs of $500. The Company did not sell any shares, and thus did not receive any proceeds under this program, for the year ended December 31, 2022**.**

Note 11. Stock-Based Compensation

2017 Equity Incentive Plan

The Company's 2017 Plan became effective in August 2017. Following the effective date of the Company's 2020 Plan, the Company ceased granting awards under the 2017 Plan, however, the terms and conditions of the 2017 Plan continue to govern any outstanding awards granted thereunder.

2020 Incentive Award Plan

The Company's 2020 Plan was approved and became effective at the Company's 2020 annual meeting of stockholders on May 20, 2020, and unless earlier terminated by the Board of Directors, will remain in effect until March 26, 2030. The 2020 Plan originally authorized for issuance the sum of (i) 911 shares of the Company's common stock and (ii) 233 shares of the Company's common stock, which represents the number of shares that remained available for issuance under the 2017 Plan immediately prior to the approval of the 2020 Plan by the Company's stockholders. Any shares of common stock which, immediately prior to the approval of the 2020 Plan by the Company's stockholders, were subject to awards granted under the 2017 Plan that are forfeited or lapse unexercised and are not issued under the 2017 Plan will increase the number of shares of common stock available for grant under the 2020 Plan. In addition, the number of shares available for issuance under the 2020 Plan will increase on the first day of each calendar year, beginning January 1, 2021 and ending on and including January 1, 2030, by a number of shares equal to the lesser of (A) 4% of the aggregate number of shares of the Company's common stock outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of shares of common stock as determined by the Board of Directors. The shares available for issuance under the 2020 Plan increased by 1,119 shares and 977 shares on January 1, 2022 and 2021, respectively.

Stock-based awards granted under the 2020 Plan have a term of ten years. The vesting schedule of all awards granted under the 2020 Plan is determined by the Board of Directors, which is generally four years.

As of December 31, 2022, there were 599 shares available to be granted under the 2020 Plan.

Restricted stock units

The table below summarizes activity relating to RSUs.

	Number of shares
Outstanding as of January 1, 2022	—
Granted	122
Forfeited	(3)
Outstanding as of December 31, 2022	119

In 2022, the Company granted 122 time-based RSUs to certain employees and consultants. The majority of RSUs granted to employees vest over four years, with 25% vesting at the one-year anniversary of the grant date and the balance vesting ratably over the remaining 12 quarters of the vesting period. 25 RSUs granted to employees in May 2022 cliff-vest 100% at the one-year anniversary of the grant date. RSUs granted to a third-party consultant vest 50% on each of the first and second anniversaries of the grant date. None of the RSUs had vested as of December 31, 2022. The weighted average grant date fair value per share for the RSUs granted in March and May 2022 was $15.31 and $10.76, respectively. Unrecognized stock-based compensation expense related to these awards was $1,229 as of December 31, 2022. No RSUs were issued and outstanding as of December 31, 2021.

Profit sharing units

The table below summarizes activity relating to profits interests (the “profit sharing units” or “PSUs”).

	Number of units	Weighted average price per unit (in whole dollars)
Outstanding as of January 1, 2022	—	$ —
Granted	1,310	$ 5,506
Outstanding as of December 31, 2022	1,310	
Vested units as of December 31, 2022	220	$ 5,506

During 2022, Employee Holdings, a management holding company used to facilitate the grant of equity interests to service providers of OnkosXcel, granted 1,310 individual (not in thousands) time-based PSUs in Employee Holdings to certain employees and consultants of the Company in consideration for services provided to OnkosXcel. The PSUs represent indirect equity interests in OnkosXcel. All PSUs, other than those granted to certain executive employees of the Company, vest ratably over 48 months. PSUs granted to certain executive employees of the Company, vest ratably over 24 months.

The fair value of $4 per unit for the PSUs was estimated at the date of grant using a Black-Scholes option pricing model.

	Profit share unit valuation inputs
Expected volatility	94.6 %
Risk-free rate of interest	4.0 %
Expected dividend yield	— %
Expected term	5.8 years

Unrecognized stock-based compensation expense related to the PSUs was $4,588 as of December 31, 2022. No PSUs were issued and outstanding as of December 31, 2021.

Stock options

A summary of the Company's stock option activity for the year ended December 31, 2022, is presented below.

	Number of shares	Weighted average price per share
Outstanding as of January 1, 2022	4,000	$ 18.89
Granted	1,378	$ 14.78
Forfeited	(227)	$ 27.52
Cancelled	(102)	$ 51.86
Exercised	(167)	$ 1.69
Outstanding as of December 31, 2022	4,882	$ 17.23
Options vested and exercisable as of December 31, 2022	3,002	$ 13.75

As of December 31, 2022, the intrinsic value of options outstanding was $49,000. The intrinsic value for stock options is calculated based on the difference between the exercise prices of the underlying awards and the quoted stock price of the Company's common stock as of the reporting date.

The total intrinsic value of stock options exercised for the years ended December 31, 2022 and 2021 was $2,437 and $11,942, respectively. The total intrinsic value of stock options exercisable as of December 31, 2022 and 2021 was $40,255 and $39,794, respectively.

The weighted average grant date fair value of options granted during the years ended December 31, 2022 and 2021 was $11.62 and $28.81, respectively.

The weighted average grant date fair value of options vested as of December 31, 2022 was $10.16.

The weighted average remaining contractual life is 5.7 years for options exercisable as of December 31, 2022. The weighted average remaining contractual life was 7.0 years for options outstanding as of December 31, 2022.

Stock-Based Compensation

The fair value of options granted during the years ended December 31, 2022 and 2021 was estimated using the Black-Scholes pricing model with the following assumptions:

	Year ended December 31, 2022			Year ended December 31, 2021		
Expected term	5.5 years	-	6.1 years	5.5 years	-	6.2 years
Expected stock price volatility	92.7 %	-	99.4 %	95.0 %	-	98.0 %
Risk-free rate of interest	1.5 %	-	4.4 %	1.0 %	-	1.4 %
Expected dividend yield	0.0 %	-	0.0 %	0.0 %	-	0.0 %

In 2021, the Company began using a combination of the historical volatility of publicly traded peer companies and the limited historical information related to the Company's common stock to estimate volatility. The expected term of the awards is estimated based on the simplified method, which calculates the expected term based upon the midpoint of the term of the award and the vesting period. The Company uses the simplified method because it does not have sufficient option exercise data to provide a reasonable basis upon which to estimate the expected term. The expected dividend yield is zero percent as the Company has no history of paying dividends nor does management expect to pay dividends over the contractual terms of these options. The risk-free interest rates are determined by reference to the U.S. Treasury yield curve in effect at the time of grant, with maturities approximating the expected term of the stock options. The fair value of the underlying common stock is generally determined as the closing price of the Company's common stock on The Nasdaq Capital Market on the grant date, with consideration of whether there is material nonpublic information that could impact that estimated fair value when it is released.

The Company recognized stock-based compensation expense related to awards issued under the 2017 Plan and the 2020 Plan, as well as the PSUs, of $17,337 and $19,455 for the years ended December 31, 2022 and 2021, respectively, which were comprised as follows:

	Year ended December 31,	
	2022	2021
Research and development	$ 4,558	$ 6,657
Selling, general and administrative	12,779	12,798
Total	$ 17,337	$ 19,455

Unrecognized compensation expense related to unvested stock option awards as of December 31, 2022, was $15,483 and will be recognized over the remaining vesting periods of the underlying awards. The weighted-average period over which such compensation is expected to be recognized is 1.6 years.

2020 Employee Stock Purchase Plan

The Company's 2020 Employee Stock Purchase Plan (the "ESPP") was also approved and became effective at the Company's 2020 annual meeting of stockholders on May 20, 2020. The ESPP is designed to assist eligible employees of the Company with the opportunity to purchase the Company's common stock at a discount through accumulated payroll deductions during successive offering periods. The aggregate number of shares that may be issued pursuant to rights granted under the ESPP is 100 shares of common stock. In addition, the number of shares available for issuance under the ESPP will increase on the first day of each calendar year, beginning on January 1, 2021 and ending on and including January 1, 2030, by a number of shares of common stock equal to the lesser of (a) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of shares as determined by the Board of Directors. The number of shares that may be issued or transferred pursuant to rights granted under the component of the ESPP that is intended to qualify for favorable U.S. federal tax treatment under Section 423 of the Internal Revenue Code (the "Section 423 Component") shall not exceed 500 shares. The purchase price will be determined by the administrator of the ESPP and, for purposes of the Section 423 Component, shall not be less than 85% of the fair value

of a share on the first trading day or on the last trading day of the applicable offering period, whichever is lower. The shares available for issuance under the ESPP increased by 280 shares and 244 shares on January 1, 2022 and 2021, respectively. To date, no shares have been sold under the ESPP.

Note 12. Leases

BTI leases office space for its corporate headquarters at 555 Long Wharf Drive, New Haven, Connecticut (the "HQ Lease") under an operating lease that expires in February 2026. The Company has an option to renew the HQ Lease for one additional five-year term. Payments under the HQ Lease are fixed.

The Company also leases equipment such as copiers and information technology equipment.

The future minimum annual lease payments under operating leases, as of December 31, 2022, were as follows:

Year ending December 31,	Amount
2023	$ 372
2024	381
2025	391
2026	65
2027	—
Thereafter	—
Total lease payments	$ 1,209
Less imputed interest	(104)
Total lease liability	$ 1,105
Less current portion of lease liability	(319)
Long-term portion of operating lease liability	$ 786

The current portion of the Company's operating lease liability of $319, as of December 31, 2022, is included in other current liabilities on the Consolidated Balance Sheets.

Lease expense was $410 and $365 for the years ended December 31, 2022 and 2021, respectively.

Lease renewal options are not included in the ROU asset or lease liability.

Note 13. Employee Benefit Plan

The Company maintains a defined contribution retirement plan for its employees that complies with Section 401(k) of the Internal Revenue Code (the "401(K) Plan"). Employees are eligible to participate in the 401(K) Plan and can contribute a portion of their pay into the 401(K) Plan, subject to annual limits established by the U.S. Internal Revenue Service. Participating employees receive an employer matching contribution equal to 50% of eligible employee contributions on the first 5% of eligible compensation contributed. During the year ended December 31, 2022, employer contributions to the 401(K) Plan were $568. BTI did not offer a matching contribution to the 401(K) Plan prior to 2022.

Note 14. Fair Value Measurements

The Company groups its assets and liabilities measured at fair value in three levels based on the nature of the inputs and assumptions used to determine fair value. Refer to Note 3, *Summary of Significant Accounting Policies*, for additional information on the accounting policies related to fair value.

The carrying amounts of cash and accounts payable approximate fair value due to the short-term nature of these instruments. As of December 31, 2022 and 2021, the Company had $191,022 and $228,584, respectively, primarily in money market funds that hold U.S. government cash equivalent instruments (included in cash and cash equivalents) which were valued based on Level 1 inputs. There were no transfers between levels within the hierarchy during the years ended December 31, 2022 and 2021.

Derivative liabilities measured at fair value on a recurring basis are summarized below.

	Year ended December 31, 2022				
	Fair Value	Level 1	Level 2	Level 3	Total
Derivative liability - Equity Investment Right	$ 1,211	$ —	$ —	$ 1,211	$ 1,211
Derivative liability - OnkosXcel Warrants	1,132	—	—	1,132	1,132
Total derivative liabilities	$ 2,343	$ —	$ —	$ 2,343	$ 2,343

Derivative liabilities are comprised of the OnkosXcel Warrants and Equity Investment Right held by the Lenders. The fair value of the derivative liabilities was determined using Monte Carlo simulation models for the Equity Investment Right, and Binomial Option Pricing and Distribution models for the OnkosXcel Warrants.

The following table presents changes in Level 3 liabilities measured at fair value for the year ended December 31, 2022. Both observable and unobservable inputs were used to determine the fair value of positions that the Company has classified within the Level 3 category.

	Derivative liabilities
Balance - December 31, 2021	$ —
Addition of derivative liabilities	1,954
Change in fair value	389
Balance - December 31, 2022	$ 2,343

The change from the day one fair value of the derivative liabilities was reported in the Consolidated Balance Sheets as derivative liabilities and Consolidated Statements of Operations as other expense, net, as of and for the year ended December 31, 2022.

Inputs used to calculate the estimated fair value of the Equity Investment Right were as follows:

	Equity Investment Right
Strike price relative to volume weighted 30-day average	110.0 %
Volatility (annual)	96.1 %
Probability of exercise	90.0 %
Time period	4.2 years
Estimated premium to 30-day average	25.0 %
Discount rate	4.4 %

In estimating the fair value of the derivative liability related to the OnkosXcel Warrants, inputs included third-party fair value estimates of OnkosXcel limited liability company units along with the volatility of those units (which was set at 100% based on the historical volatility of the Company's stock, along with a peer group of comparable publicly traded companies), and the timing and probability of the relevant capital transactions occurring.

The estimated fair value of the Credit Agreement and RIFA as of December 31, 2022, were $52,670 and $30,673, respectively. Both observable and unobservable inputs were used to determine the fair value of long-term debt, which was classified within the Level 3 category.

The fair value of the BTI warrants, which is a non-recurring fair value, was determined as of the date of issuance using a Black-Scholes pricing model and the fair value of $3,245 was recorded as a component of stockholders' equity in additional-paid-in-capital in the Consolidated Balance Sheets, with the offset recorded as a discount on the amounts funded under the OFA Facilities. This non-recurring measurement is classified as a Level 3. The inputs used were a strike price of $20.04, the Company's stock price of $14.93, volatility of 95%, term of 7 years and risk-free rate of 2.95%.

Note 15. Income Taxes

There is no provision for income taxes because the Company has historically incurred operating losses and maintains a full valuation allowance against its net deferred tax assets. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of changes in valuation allowance.

For tax years beginning on or after January 1, 2022, the 2017 Tax Cuts and Jobs Act amended Section 174 of the U.S. Tax Code to eliminate current-year deductibility of research and development expenses and requires taxpayers to capitalize and amortize them over five years for research activities performed in the U.S. and fifteen years for research activities performed outside of the U.S. For the 2022 tax year, the Company capitalized $86,704 of research and development expenses. This resulted in an increase in the deferred tax asset associated with capitalized research and development of $22,764. In determining the realizability of the Company's net deferred tax asset, the Company considered numerous factors, including historical profitability, estimated future taxable income, and the industry in which it operates. Based on this information the Company has provided a valuation allowance for the full amount of its net deferred tax asset because the Company has determined that it is more likely than not that it will not be realized. The significant components of the Company's net deferred tax assets are as follows:

	December 31, 2022	December 31, 2021
Deferred tax assets:		
Federal net operating losses	$ 46,695	$ 29,157
State net operating losses	11,271	8,213
Stock options	10,705	7,461
Tax credits	10,689	7,102
Capitalized research & development	36,663	18,880
Accrued expense	2,171	1,026
Depreciation	42	17
Lease liability	290	376
Unrealized loss	103	3
Valuation allowance	(118,373)	(71,899)
Total deferred tax assets	$ 256	$ 336
Deferred tax liabilities:		
Right-of-use assets	$ (256)	$ (336)
Total deferred tax liabilities	$ (256)	$ (336)
Net deferred tax asset (liability)	$ —	$ —

The income tax benefit for the year ended December 31, 2022 differed from the amounts computed by applying the U.S. federal income tax rate of 21% to loss before tax benefit as a result of nondeductible expenses, tax credits generated and increases in the amount of the Company's valuation allowance.

A reconciliation between the Company's effective tax rate and the federal statutory rate are as follows:

	Year ended December 31,	
	2022	2021
Federal statutory rate	21.0 %	21.0 %
Stock based compensation	(0.4)%	0.1 %
Federal tax credits	2.1 %	2.1 %
State taxes	4.2 %	5.8 %
Other	1.1 %	(0.7)%
Valuation allowance	(28.0)%	(28.3)%
	— %	— %

As of December 31, 2022, the Company had approximately $222,355 of gross federal and $214,489 of gross state net operating loss (“NOL”) carryforwards. If not utilized, the federal and state NOL carryforwards will begin to expire in 2037. The federal NOL of $219,709 incurred after December 31, 2017, will be carried forward indefinitely. The utilization of such NOL carryforwards and realization of tax benefits in future years depends predominantly upon having taxable income. The Company also has approximately $10,013 of federal orphan drug and research development credits which will begin to expire in 2037 if not utilized.

Utilization of the NOL and research tax credit carryforwards may be subject to a substantial annual limitation due to ownership limitations that have occurred or that could occur in the future, as required by section 382 of the U.S. Tax Code, as well as similar state and foreign provisions. These ownership changes may limit the amount of the NOL and research credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change," as defined by Section 382 of the U.S. Tax Code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock by certain stockholders or public groups.

Entities are also required to evaluate, measure, recognize and disclose any uncertain income tax positions taken on their income tax returns. The Company has analyzed its tax positions and has concluded that as of December 31, 2022, there were no uncertain positions. The Company's U.S. federal and state NOLs have occurred since its inception in 2017 and as such, tax years subject to potential tax examination could apply from that date because the utilization of NOLs from prior years opens the relevant year to audit by the U.S. Internal Revenue Service and/or state taxing authorities. BTI did not have any unrecognized tax benefits and has not accrued any interest or penalties for the years ended December 31, 2022 and 2021.

Note 16. Net Loss Per Share

Basic and diluted net loss per share are as follows:

	Year ended December 31,	
	2022	2021
Net loss (numerator)	$ (165,757)	$ (106,931)
Weighted average shares (denominator)	28,015	26,373
Basic and diluted net loss per share	$ (5.92)	$ (4.05)

Potentially dilutive securities outstanding consists of stock options and RSUs. The Company had common stock equivalents outstanding as of December 31, 2022 and 2021 of 5,001 and 4,000 shares, respectively.

Note 17. Commitments and Contingencies

From time to time, in the ordinary course of business, the Company may be subject to litigation and regulatory examinations as well as information gathering requests, inquiries and/or investigations. The Company is not currently subject to any matters where it believes there is a reasonable possibility that a material loss may be incurred. As of December 31, 2022, there were no matters which would have a material impact on the Company’s financial results.

In April 2022, the Company signed a commercial supply agreement that requires minimum annual payments for the first three years of the agreement that in aggregate total $10,000 for the three-year period.

Note 18. Subsequent Events

As of March 15, 2023, the Company sold 756 shares under the Sale Agreement with Jefferies in the first quarter of 2023 for net proceeds of $23,917, net of issuance costs of $740.

Exhibit 21.1

Subsidiaries

OnkosXcel Therapeutics, LLC

OnkosXcel Employee Holdings, LLC

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 Nos. 333-240118 and 333-265277) of BioXcel Therapeutics, Inc., and

(2) Registration Statements (Form S-8 Nos. 333-235282, 333-238580 and 333-266922) pertaining to the 2017 Equity Incentive Plan and the 2020 Incentive Award Plan and 2020 Employee Stock Purchase Plan of BioXcel Therapeutics, Inc.

of our report dated March 15, 2023, with respect to the consolidated financial statements of BioXcel Therapeutics, Inc. included in this Annual Report (Form 10-K) of BioXcel Therapeutics, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young, LLP

Stamford, Connecticut

March 15, 2023

Exhibit 31.1

CERTIFICATIONS

I, Vimal Mehta, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2022, of BioXcel Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2023

By: /s/ Vimal Mehta
Vimal Mehta, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Richard Steinhart, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2022, of BioXcel Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2023

By: /s/ Richard Steinhart
Richard Steinhart
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of BioXcel Therapeutics, Inc. (the "Company") for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 15, 2023

By: /s/ Vimal Mehta
Vimal Mehta, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of BioXcel Therapeutics, Inc. (the "Company") for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 15, 2023

By: /s/ Richard Steinhart
Richard Steinhart
Chief Financial Officer
(Principal Financial Officer)