2021 ANNUAL REPORT

bioxcel therapeutics®

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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, 2021
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. ☐

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, 2021, 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 $550,896,639 (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 27,980,345 shares of our common stock outstanding at March 1, 2022.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2022 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, 2021, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our plans relating to clinical trials for BXCL501, BXCL701 and our other product candidates;
- our plans for 505(b)(2) regulatory path approval;
- 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 for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing;
- 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. Factors that may cause actual results to differ materially from current expectations include, among other things, 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. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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.

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 sections 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 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 never generated any product revenues, 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 limited experience in drug discovery and drug development, and we have never had a drug approved.

- In the near term, we are dependent on the success of BXCL501 and BXCL701. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize BXCL501, BXCL701 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.

- 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 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, if any.

- BioXcel's approach to the discovery and development of product candidates based on EvolverAI 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 FDA 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.

- Even if we obtain regulatory approval for BXCL501, BXCL701 or any product candidate, we will still face extensive and ongoing regulatory requirements and obligations and any product candidates, if approved, may face future development and regulatory difficulties.

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

- Even if we obtain regulatory approvals to commercialize BXCL501, BXCL701 or our other product candidates, our product candidates may not be accepted by physicians or the medical community in general.

- We continue to depend on BioXcel 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 we intend to rely on third parties to produce commercial supplies of any 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.

- 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.

- 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.

PART I

Item 1. Business

Overview

We are a clinical stage biopharmaceutical company utilizing artificial intelligence approaches to develop transformative medicines in neuroscience and immuno-oncology. Our drug re-innovation approach leverages existing approved drugs and/or clinically validated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indices. We believe that this differentiated approach has the potential to reduce the cost and time of drug development in diseases with a substantial unmet medical need.

Our two most advanced clinical development programs are BXCL501, an investigational, proprietary, orally dissolving, sublingual thin film formulation of the adrenergic receptor agonist dexmedetomidine, or Dex, for the treatment of agitation resulting from neuropsychiatric disorders, and BXCL701, an investigational orally administered systemic innate immune activator for the treatment of castration resistant prostate cancer and advanced solid tumors that are refractory or treatment naïve to checkpoint inhibitors.

Impact of COVID-19 Pandemic

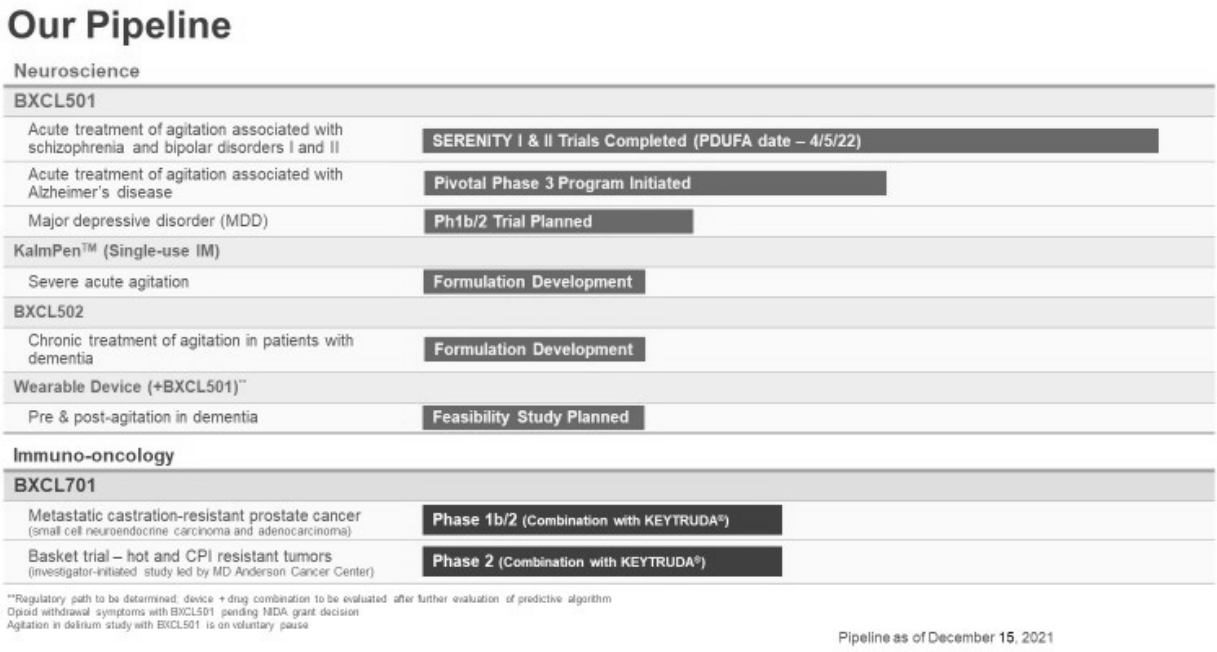
During the first quarter ended March 31, 2020, and continuing through December 31, 2021, the novel coronavirus disease, or COVID-19, was declared a pandemic and spread to multiple regions across the globe, including the United States and Europe. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen.

To date, we have taken steps in line with guidance from the U.S. Centers for Disease Control and Prevention ("CDC") and the State of Connecticut to protect the health and safety of our employees and the community. In particular, we implemented a work-from-home policy for all employees and have restricted on-site activities to certain chemical, manufacturing and control ("CMC") and clinical trial activities. We continue to assess the impact of the COVID-19 pandemic to best mitigate risk and continue the operations of our business. Beginning late in the second quarter of 2020, we began to slowly bring our staff, in very limited numbers, back to our office. This modified return-to-work approach is continuing into 2022. We have taken steps to protect our workforce and have instituted strict work rules to protect our employees.

We continue to work closely with our clinical sites to monitor the potential impact of the evolving COVID-19 pandemic. We remain committed to our clinical programs and development plans. Other than our Phase 2 clinical trial evaluating BXCL501 in patients with delirium, through December 31, 2021, we have not experienced any significant delays to our ongoing or planned clinical trials, except for challenges in accessing elderly care facilities and ICU settings; however, this could rapidly change.

Our Clinical Programs

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



Our Strategy

Our goal is to become the leading AI-enabled neuroscience company while further developing our immuno-oncology assets. We continue to evaluate all strategic options available to us for these assets which could include licensing, partnering, co-commercialization or a spin-out. The key elements to achieving these goals are as follows:

Neuroscience

- **Advance BXCL501, a proprietary, orally dissolving thin film formulation of dexmedetomidine, or Dex, a selective α_{2a} adrenergic receptor agonist,** targeting symptoms from stress-related behaviors such as agitation and opioid withdrawal symptoms. BXCL501 is our most advanced neuroscience clinical program, currently being developed for the acute treatment of agitation related to schizophrenia, bipolar disorders, Alzheimer's disease and delirium, the symptoms associated with opioid withdrawal, and as an adjunctive treatment for major depressive disorder ("MDD") in conjunction with the use of Selective Serotonin / Norepinephrine Reuptake Inhibitors ("SS/NRIs"). We have submitted a New Drug Application (NDA) utilizing the Section 505(b)(2) pathway for BXCL501 for the acute treatment of agitation associated with schizophrenia and bipolar disorders I and II. The United States Food and Drug Administration ("FDA") filed the application for review and assigned an April 5, 2022, Prescription Drug User Fee Act ("PUDFA") goal date.
    - **Neurological and Psychiatric Disorders.** We believe that BXCL501, if approved, 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 where agitation is a symptom of the condition or underlying disease, including:
  - As an adjunctive treatment for MDD;
  - Opioid withdrawal (RELEASE trial);
  - Delirium (PLACIDITY trial); and
  - Post-traumatic stress disorder ("PTSD").

Pipeline Opportunities for Franchise Expansion

In December 2020, the VA Connecticut Healthcare System and Yale University Medical School were awarded a grant by the U.S. Department of Defense's Congressionally Directed Medical Research Programs to evaluate BXCL501 in patients suffering from PTSD as well as alcohol use disorder. We plan to investigate BXCL501 as a potential chronic treatment for PTSD.

We continue to explore the potential for a wearable device to measure early signs of agitation in patients who are consistent with the patient groups we are evaluating in BXCL501 clinical trials. Feasibility studies demonstrated that patients were able to wear these devices and that these devices were able to transmit data to our service vendor. Along with our service vendor, we are developing methods to use these data in an effort to construct algorithms designed to predict when a patient is becoming agitated. The goal of this program is to establish a predictive algorithm that would allow providers to treat patients before they become highly agitated. A study in healthy volunteers that are mildly agitated is scheduled to begin in Q1, 2022.

We are advancing our preparations for commercial and launch readiness in preparation for the potential approval of our NDA for BXCL501 by the FDA. We are optimizing the design and recruitment of our sales force and market access and pricing strategy for the potential commercial launch of BXCL501 for the acute treatment of agitation associated with schizophrenia and bipolar disorders I & II. This work will be a crucial foundation to launching additional potential follow-on indications, paving the way for our expanding neuroscience business.

During the second half of 2021, we fully launched our unbranded disease education campaign to promote awareness around the treatment of agitation in schizophrenia and bipolar disorders. In addition, we fully deployed our Medical Science Liaison and Medical Managed Care teams who actively engaged with healthcare professionals and payors to provide key insights to support our commercial strategy.

If BXCL501 is approved outside the United States we would consider launching the product through collaborations with third parties.

We recently identified and initiated the development of a second neuropsychiatric product candidate, BXCL502. 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, including Alzheimer's disease. The active pharmaceutical ingredient ("API") underlying BXCL502 is designed to be a potent and selective antagonist of a G-protein coupled receptor ("GPCR") that affects serotonergic signaling in the brain. Our preclinical data and machine learning results suggest BXCL502 has the potential to treat agitation and stress related neuropsychiatric symptoms in dementia. In previously published third party clinical trial data, daily administration of the API of BXCL502 demonstrated improvement in agitation using a well-established, clinically validated

symptom scale. Formulation and clinical development planning are currently underway with BXCL502.

Immuno-Oncology

BXCL701 is a potential first-in-class, oral, small-molecule immunomodulator designed to stimulate both the innate and acquired immune systems by inhibiting DPP 8/9. DPP 8/9 behave as "checkpoints" of pyroptosis and inflammasome activation. We believe that BXCL701, if successfully developed and approved, may establish a differentiated immuno-oncology platform by modulating multiple steps in the cancer immunity cycle and, when combined with checkpoint inhibitors and/or immune activating agents, may be able to convert immuno-resistant ("cold") tumors to immuno-sensitive ("hot") tumors.

- **Complete BXCL701 Phase 2 trials to evaluate its potential for the treatment of castrate resistant cancer ("CRPC"), including the neuroendocrine ("NEPC") variety.**

    - **NEPC (Orphan Segment of Prostate Cancer and Castrate Resistant Prostate Cancer).** BXCL701 was previously studied in multiple clinical trials and demonstrated single agent anti-tumor activity in melanoma, an immune-sensitive tumor. In April 2020, we announced the initiation of the Phase 2 efficacy portion of the Phase 1b/2 trial evaluating BXCL701 in combination with KEYTRUDA® (pembrolizumab, a PD-1 inhibitor) for NEPC. In addition to the efficacy cohort in NEPC patients, in August 2020, we opened a separate cohort for CRPC patients who have failed taxane-based chemotherapy and up to two lines of second-generation androgen pathway blockers. Topline results from the Phase 1b portion of this trial were presented at the American Society of Clinical Oncology Genitourinary Symposium in February 2021. Interim data from the Phase 2 portion of the study were also presented at the European Society for Medical Oncology conference in September 2021. We reported updated interim data from the Phase 2 portion of this trial in NEPC and adenocarcinoma cohorts at the American Society of Clinical Oncology ("ASCO") Genitourinary Cancers Symposium ("ASCO-GU") in February 2022.

    - **Basket Trial.** BXCL701 is being evaluated in an open-label Phase 2 basket trial led by MD Anderson. The investigator led study is designed to evaluate the response rate of orally administered BXCL701, combined with Pembrolizumab (KEYTRUDA®) in patients with advanced solid cancers. The study will evaluate patients who are naïve to checkpoint therapy and those who are refractory to checkpoint therapy. Interim data were presented at the June 2021 ASCO annual meeting. In the first half of 2022, we expect to present additional interim efficacy data from the trial.

    - **Potential for Expedited Review Programs.** Given that these indications represent high unmet medical needs with few treatment options, we intend to pursue breakthrough therapy designation and accelerated approval for NEPC.

    - **Additional Indications.** We believe BXCL701 may be active at multiple stages of the cancer immunity cycle and therefore, we believe BXCL701 offers a "pipeline in a product" platform given its potential for evaluation across other cancers. BXCL701 was granted orphan drug designation for the treatment of acute myeloid leukemia in September 2019, its fourth orphan drug designation in addition to pancreatic cancer, melanoma, and soft tissue sarcoma. We believe existing preclinical (and clinical) evidence supports the combination of BXCL701 with checkpoint inhibitors and/or agents that act on "co-stimulatory" pathways within immune effector cells. Moreover, we believe agents that stimulate antibody-dependent cell mediated cytotoxicity ("ADCC"), or cell-based therapies such as chimeric antigen receptor T cell, therapy, oncolytic viruses or therapeutic vaccines all represent potential combination with BXCL701.

Other

- **Identify biomarkers to select patients who we believe have the highest likelihood to respond to our product candidates. Predicting optimal drug responses in patients requires the identification and validation of predictive biomarkers.** We believe that our ability to identify patient subsets most likely to

respond to our product candidates will increase the clinical benefit to patients and improve the probability of success of our clinical trials. The indications for our lead product candidate BXCL701 were chosen in part because they are known to overexpress dipeptidyl peptidase, or DPP 8/9, and fibroblast activation protein, or FAP. Our planned proof-of-concept clinical trial of BXCL701 will retrospectively examine biomarkers related to its molecular and cellular targets to identify those that may correlate with clinical efficacy and increase our likelihood of success.

- **Maximize the commercial potential of our product candidates.** We have worldwide development and commercialization rights to BXCL501, BXCL502, and BXCL701. If BXCL501 and BXCL701 are approved in the United States, we are developing plans to build a specialty sales force in the United States for BXCL501 and considering other opportunities to collaborate with third parties to maximize the potential of our product candidates.

- **Enhance our R&D pipeline by leveraging our therapeutic area expertise with our growing internal capabilities to identify, develop and commercialize new product candidates in neuroscience and immune oncology.** In addition to our leading clinical programs and our emerging and future pipeline, we have identified several potential product candidates and intend to select our next clinical program from among such candidates. We have established translational and development expertise, which we believe will help us advance the present and future product candidates in these fields. We may also opportunistically in-license additional product candidates identified through our AI platform approach within our core areas of expertise.

Our Novel Drug Re-Innovation Approach

We aim to develop and implement holistically throughout the drug development process an artificial intelligence ("AI") eco system designed to rapidly identify drugs that engage novel targets related to our key focus areas in neuroscience and immuno-oncolgy. Our in-house, uniquely integrated AI -to -drug -development capability is complemented by BioXcel LLC's services and technology. 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 also provide the basis for stronger intellectual property positions. The AI team works closely with business development 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 that are 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 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 identifying combinations that we believe may have a higher probability of success.

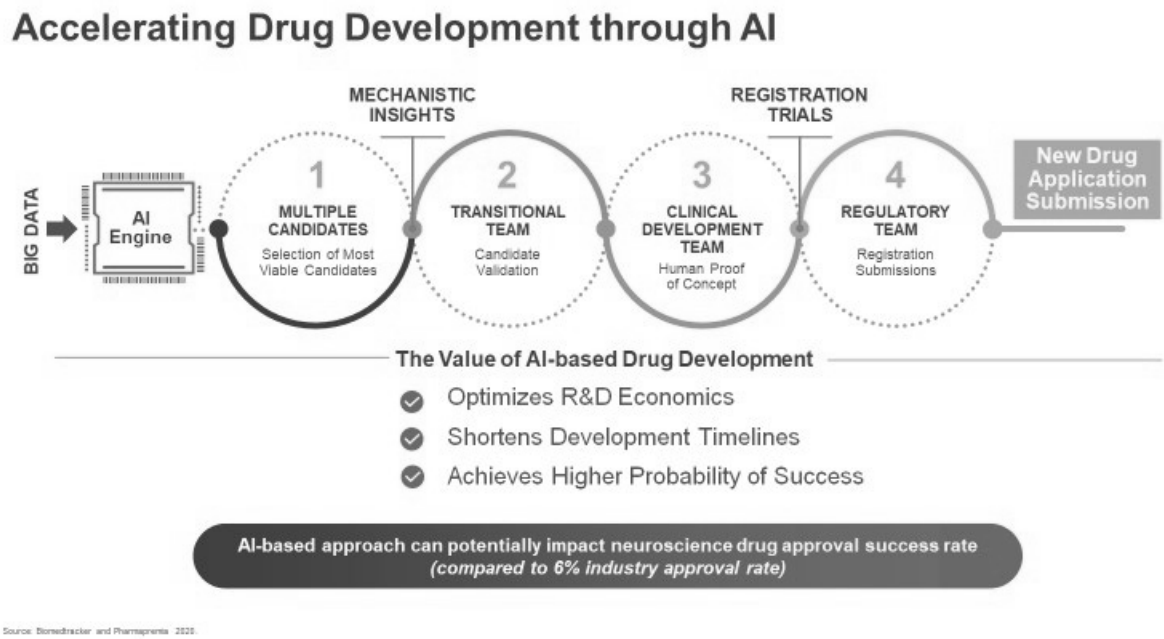
Traditional drug development is plagued with low success rates (13.8%, according to an MIT study of 186,000 trials from January 2000 to October 2015), long drug development cycles (10-15 years, according to PhRMA Key Facts 2016), and exorbitant development costs ($2.6 billion per drug, according to PhRMA Key Facts). Furthermore, many serious diseases continue to go unaddressed due to limitations of the current drug discovery paradigm. The pharmacological space spans more than 27,000 active pharmaceutical agents, and 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 need and recoupment of 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. They 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 sacrificing 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 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 of 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:



Source: Biomedtracker and Pharmaprenia 2020.

We continue to integrate and evolve our neuroscience and immuno-oncology AI machine learning and drug discovery and development platform. Our platform has led to the identification and rapid development of BXCL501, leading to the submission of our first NDA 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.

BXCL501 Neuroscience Program

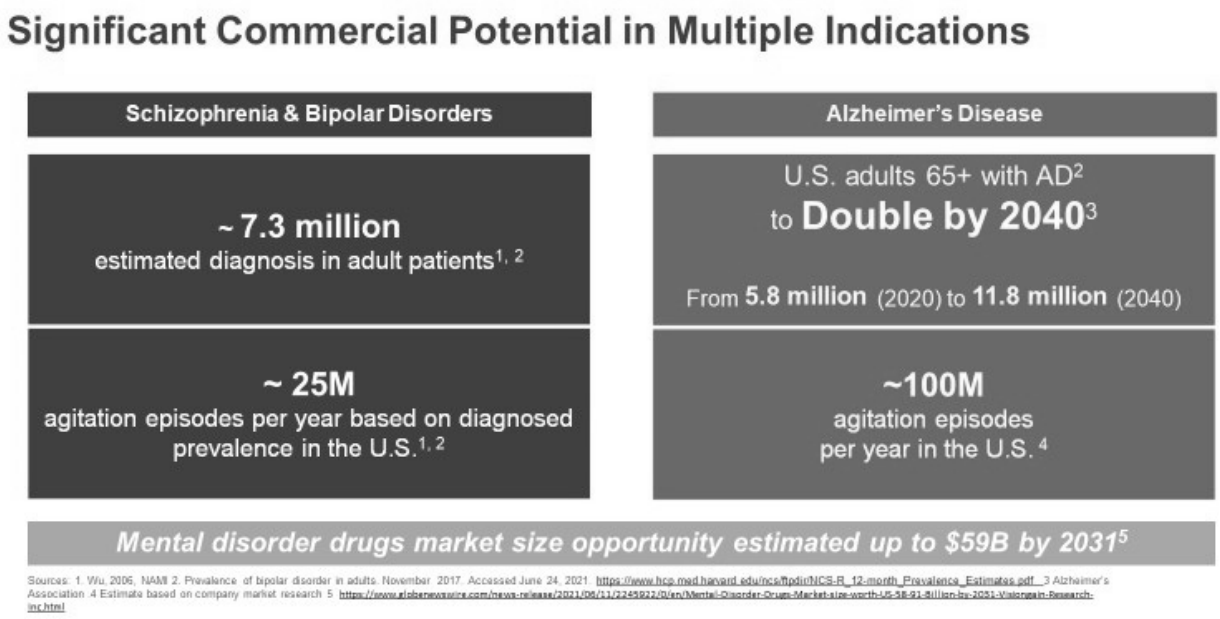
Overview

BXCL501 is an investigational, proprietary, orally dissolving, thin film formulation of dexmedetomidine (Dex), a selective alpha-2 receptor agonist, targeting symptoms from stress-related behaviors such as agitation and opioid withdrawal symptoms. BXCL501 is our most advanced neuroscience clinical program, currently being developed for the acute treatment of agitation related to schizophrenia, bipolar disorders, dementia (Alzheimer's disease) and delirium, the symptoms associated with opioid withdrawal as well as for the adjunctive treatment of MDD in conjunction with the use of SSRIs or SNRIs. 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, which 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 (psychomotor agitation) 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 sometimes 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 of time.

With the agitation issues associated with schizophrenia and bipolar disease coupled with a fast growing elderly population who are potentially likely to experience agitation associated with Alzheimer's disease, the difficulties and expenses of acute treatment of agitation are expected to grow significantly. Based on our market research, estimates indicate that by 2031 drugs for mental disorders could be up to $59 billion. Below are estimated statistics associated with these indications.



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 dehumanizes patients and can cause trauma that could have long-term impact on the patient. 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 can contribute 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. Non-adherence 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 thin film offers compliance advantages as it will prevent patients from avoiding treatment.

There is precedent for FDA approval of a non-invasive therapy for the acute treatment of agitation. In 2012, Adasuve®, an inhaled version of the antipsychotic loxapine, became the first approved non-invasive acute treatment for agitation in patients with schizophrenia and bipolar 1 disorder. The use of Adasuve has been limited due to a risk management program and the risk of bronchospasm. Adasuve also has a high incidence of side effects. Upon launch, Adasuve was priced at $145 per dose.

The sublingual or buccal route of administration is an accepted alternative to oral administration of drug delivery to the central nervous system, or CNS, when rapid onset or more controlled delivery is required. Currently, there are six products that are approved for thin-film administration. 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 have developed BXCL501 as a differentiated sublingual thin film dosage form of Dex, which we believe, if approved, may offer benefits such as ease of use and quick absorption for rapid therapeutic effects.

Mechanism of Action: α_{2a} Adrenergic Receptor and NE Role in Acute Agitation

BXCL501 is designed to be easily administered and to have a rapid onset of action. We believe that BXCL501, with its differentiated pharmacology and ease of administration, if approved, 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 United States 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 United States 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 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 ("RASS") 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 thin film and at much lower doses will allow for ease of administration in settings where rapid acute treatment of agitation is needed.

BXCL501 Clinical Trials

SERENITY I and SERENITY II

In July 2020, we announced topline results from the SERENITY I and II pivotal trials, which showed that treatment with BXCL501 was well-tolerated and resulted in clinically meaningful reductions in agitation in schizophrenia and bipolar disorder I and II patients. In October 2020, we held a pre NDA meeting with the U.S. Food and Drug Administration ("FDA") to discuss the content and format of our anticipated NDA submission. The FDA also agreed to a rolling review of our NDA, allowing us to submit completed sections of the application early. On March 5, 2021, we completed the rolling submission of our NDA to the FDA. In May 2021, we announced the FDA had notified us that our NDA submission was accepted for filing. The FDA assigned a PDUFA goal date of January 5, 2022. In December 2021, we announced the extension of the FDA review period of our NDA to April 5, 2022. We also have plans underway to submit a Marketing Authorization Application ("MAA") to the European Medicines Agency ("EMA") for BXCL501 for the acute treatment of agitation associated with schizophrenia and bipolar disorders I & II in the first half of 2022.

TRANQUILITY and TRANQUILITY II and III

In January 2021, we announced topline results from the TRANQUILITY trial, a Phase 1b/2 randomized, placebo-controlled, adaptive ascending dose-finding study that enrolled 54 patients with agitation related in dementia., including Alzheimer's disease. Patients received BXCL501 at either 30mcg (n=16), 60mcg (n=20), 90 mcg (n=4) or placebo (n=14). Overall, BXCL501 was well tolerated and demonstrated statistically significant, clinically meaningful, rapid, and durable reductions in agitation with the 60 mcg dose as measured by multiple rating scales.

The trial's primary endpoint was to evaluate safety and tolerability in elderly demented patients experiencing an acute episode of agitation. During the study, BXCL501 was well-tolerated and no severe or serious adverse events were reported. The most common adverse event was somnolence characterized as either mild (55% for 60 mcg, 50% for 30 mcg and 7.1% for placebo) or moderate (5% for 60 mcg and 0% for both 30 mcg and placebo), followed by hypotension (10%, 0%, 0%), orthostatic hypotension (5%, 6.3%, 0%) and dizziness (5%, 6.3% and 0%). There were no reported cases of syncope or falls in any of the patients studied. For the same dose, higher exposure levels of BXCL501 were observed in this elderly patient population compared to earlier trials in younger patient populations.

The trial met its secondary efficacy endpoints with the 60 mcg dose compared to placebo in all three agitation scales: the Positive and Negative Syndrome Scale-Excitatory Component Score ("PEC" or "PANSS-EC") the Pittsburgh

Agitation Scale ("PAS"), and the Modified Cohen -Mansfield Inventory ("Mod-CMAI"). Treatment with BXCL501 demonstrated statistically significant and clinically meaningful reductions in total scores at two hours post-dosing (PEC $p=0.0011$; PAS $p<0.0001$; Mod-CMAI $p<0.001$; PEC response rate = 70%), numerical separation from placebo in PEC total score as early as 30 minutes with statistically significant reductions on both PEC and PAS at 60 minutes lasting 8 hours after treatment.

Additional statistically significant reductions with the 60 mcg dose compared to placebo at the 2 hours post-dosing were observed with the Agitation and Calmness Scale ("ACES") (ACES $p=0.0006$) and Clinical Global Impression-Improvement Scale (CGI $p<0.0001$, 90% responder rate).

The 30 mcg dose cohort showed numerical improvements across all scales.

On March 3, 2021, we announced that following a routine quality control review of the Company's TRANQUILITY study data, the Company discovered that two patients dose assignments were mis-categorized within the 30 mcg cohort at the clinical site. After moving the two patients data into their appropriate placebo and 30 mcg treatment groups, the data from the 30 mcg cohort were re-analyzed, resulting in the 30 mcg dose crossing over to statistical significance at the two hour time point, as measured by PEC: $p=0.0149$; PAS: $p=0.0195$; and Mod-CMAI: $p=0.0364$.

The Company also announced that it extended the TRANQUILITY I trial to initiate a 46 patient (1:1 randomization) multicenter, double-blind placebo-controlled expansion study investigating a 40 mcg dose cohort of BXCL501. Pharmacokinetics and pharmacodynamics modeling of BXCL501 data from the TRANQUILITY trial was supportive of evaluating the efficacy of a 40 mcg dose. Results of this expansion are expected to provide additional insights to support the Company's clinical development strategy directed at all segments of the dementia market.

On March 15, 2021 we announced that BXCL501 was granted Breakthrough Therapy designation from the FDA for the acute treatment of agitation associated with dementia. This designation is intended to expedite the development and review of certain product candidates designed to treat serious or life-threatening diseases or conditions, and the designation enables increased interaction and guidance from the FDA.

On December 15, 2021, after our initial Breakthrough Therapy designation meetings with FDA, we announced the initiation of our program to evaluate BXCL501 for the treatment of acute agitation associated with dementia in Alzheimer's patients. 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 illness in assisted living or residential facilities and nursing homes.

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

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

- TRANQUILITY II will enroll patients with mild to moderately severe dementia in assisted living or residential facilities who generally require minimal assistance with activities of daily living. TRANQUILITY III will enroll patients in nursing homes with moderate to severe dementia who require moderate or greater assistance with their activities of daily living.

- The studies are designed to assess agitation as measured by the changes from baseline in the PEC and PAS total scores. The primary efficacy endpoint for both studies will be the change in PEC total score from baseline measured at two hours after the initial dose and subsequent doses.

- 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 and efficacy of BXCL501 in continued use.

RELEASE

The RELEASE trial was a multicenter, randomized, double-blind, placebo-controlled, ascending dose Phase 1b/2 trial designed to evaluate the safety, pharmacokinetics, tolerability, and efficacy of BXCL501 administered twice daily for 7 days in patients experiencing symptoms of opioid withdrawal.

In March 2021, we announced RELEASE top line results. The trial's primary objective was to evaluate safety and tolerability of twice daily dosing of BXCL501 for 1 week. BXCL501 was well tolerated, with no severe or serious adverse events reported across all doses evaluated.

With respect to retention, a secondary endpoint, the study showed that patients in multiple dose cohorts treated with BXCL501 had numerical improvements in retention rates, a key goal of opioid withdrawal treatment, compared to placebo. The 120 mcg and 180 mcg dose groups showed 42% and 52% rates of retention at day 6 of BXCL501 treatment, respectively, versus 24% for placebo, though these differences were not statistically significant. However, the results also showed that, of the 87% of patients who had fentanyl in their systems upon entry, with greater than 50% remaining fentanyl positive following the morphine stabilization phase of 5 days. Consequently, withdrawal symptoms were not equivalent across various dose cohorts, suggesting that morphine did not stabilize or 'normalize' withdrawal symptoms in these patients. Efficacy measures, including assessment of patients' symptoms of acute opioid withdrawal following the morphine maintenance phase with the Clinical Opiate Withdrawal Scale ("COWS") and the Short Opiate Withdrawal Scale of Gossop ("SOWS-Gossop") were secondary objectives of the trial. Improvements were not observed in SOWS-Gossop") or COWS total scores in the BXCL501 treatment arms compared to placebo. The Company believes that the high prevalence of fentanyl, and its extended washout may have contributed to the lack of normalization of withdrawal during morphine maintenance could have confounded results and made them difficult to interpret.

We believe the favorable tolerability results observed in multiple dose regimens within the RELEASE trial provides valuable insights that support investigation across additional indications and treatment settings.

PLACIDITY

In October 2020, we announced that we had received authorization to proceed under our Investigational New Drug ("IND") application from the FDA for treatment of patients with agitation associated with delirium in intensive care units, including patients with COVID-19 and on February 25, 2021, we announced the initiation of the Phase 2 PLACIDITY trial of BXCL501. This program is intended to provide a potential synergy with the medical and commercial infrastructure being developed to support our first two indications.

The PLACIDITY trial is a multicenter, randomized, double-blind, placebo-controlled, ascending dose-finding, adaptive Phase 2 study designed to evaluate the safety, efficacy, and pharmacokinetics of BXCL501 in intensive care unit adult patients experiencing delirium related agitation, including COVID-19 patients. Approximately 20 patients will be randomized into each sequential ascending dose cohort of BXCL501 (starting doses of 120 ug, 180 ug, 240 ug, or 300 ug), or matching placebos to determine an optimal starting dose that could effectively and safely reduce agitation. Elderly delirium patients (65 years or older) in these cohorts will receive half the dose. The primary endpoint is the reduction in agitation measured by at least a 2-point drop in the Richmond Agitation Sedation Scale ("RASS") at two hours post BXCL501 administration. The secondary endpoint is the earliest time at which a 2-point drop is seen in RASS after BXCL501 administration. An exploratory endpoint of this trial will be to determine the overall clinical improvement after drug administration using the Clinical Global Impression – Improvement Scale ("CGI-I").

Agitation associated with delirium is a serious condition that affects patients in many hospital settings: ICUs, surgical & medical wards, and emergency departments. Currently, there are no FDA-approved medications for delirium or agitation associated with delirium.

PLACIDITY enrollment was voluntarily paused, and continues to be paused, to assess challenges posed in opening relevant clinical sites and enrolling delirium patients in the ICU settings, including as a result of the burden COVID-19 has placed on the ICU.

The Company and its collaborators, the VA Connecticut Healthcare System and the Yale University Medical School, are evaluating BXCL501 in patients suffering from PTSD related to alcohol and substance abuse disorder ("ASUD"). Yale University Medical School was awarded a grant by the U.S. Department of Defense's ("DOD") Congressionally Directed Medical Research Programs ("CDMRP"). The Company is investigating BXCL501 as a potential chronic treatment for patients with these conditions.

Given the significant market opportunities available to us developing BXCL501 for the treatment of agitation in patients with Alzheimer's disease and MDD, we have determined it is the best interest of all stakeholders to focus our efforts in those disease areas and have decided to de-emphasize our opioid withdrawal and delirium indications.

PEDIATRIC STUDY

In June 2021, we initiated a global clinical trial designed to evaluate the safety and efficacy of BXCL501 in agitation associated with pediatric schizophrenia and bipolar disorder. The multisite, double-blind, placebo controlled, parallel group trial will enroll patients with schizophrenia, schizoaffective disorder, bipolar I and bipolar II disorder. Similar to the SERENITY I and II trials, the primary endpoint is the change from baseline PEC total score at 2 hours. The trial has been initiated in the U.S. and enrollment is ongoing.

Major Depressive Disorder

We have recently expanded our programs to evaluate BXCL501 as an adjunctive treatment for MDD. We expect that the initial clinical study in this program will be a double-blind, placebo-controlled, multiple ascending dose trial to evaluate the safety and tolerability of twice daily doses of BXCL501 in healthy volunteers. A Phase 2 proof of concept study is planned to evaluate whether daily adjunctive use of BXCL501 provides a more rapid initial clinical antidepressant response than placebo when initiating SSRI or SNRI alone. We are preparing to submit an IND to the FDA and if allowed to proceed by the FDA, expect to initiate the first clinical trial in the first half of 2022.

BXCL701, DPP 8/9 Inhibitor for the treatment of Castration-Resistant Prostate Cancer

BXCL701 is a potential first-in-class, oral, small-molecule immunomodulator designed to stimulate both the innate and acquired immune systems by inhibiting DPP 8/9. DPP 8/9 behave as "checkpoints" of pyroptosis and inflammasome activation. We believe that BXCL701, if successfully developed and approved, may establish a differentiated immuno-oncology platform by modulating multiple steps in the cancer immunity cycle and, when combined with checkpoint inhibitors and/or immune activating agents, may be able to convert immuno-resistant ("cold") tumors to immuno-sensitive ("hot") tumors.

Clinically, BXCL701 has been evaluated in more than 700 healthy subjects and cancer patients across multiple clinical trials, which provided evidence regarding tolerability, proof of mechanism, and single agent anti-tumor activity. In the latter case, single agent activity was seen in melanoma patients, an immune sensitive tumor. While providing evidence regarding the safety profile of the drug, these clinical studies also identified a maximum tolerated and recommended Phase 2 dose to use in future clinical trials.

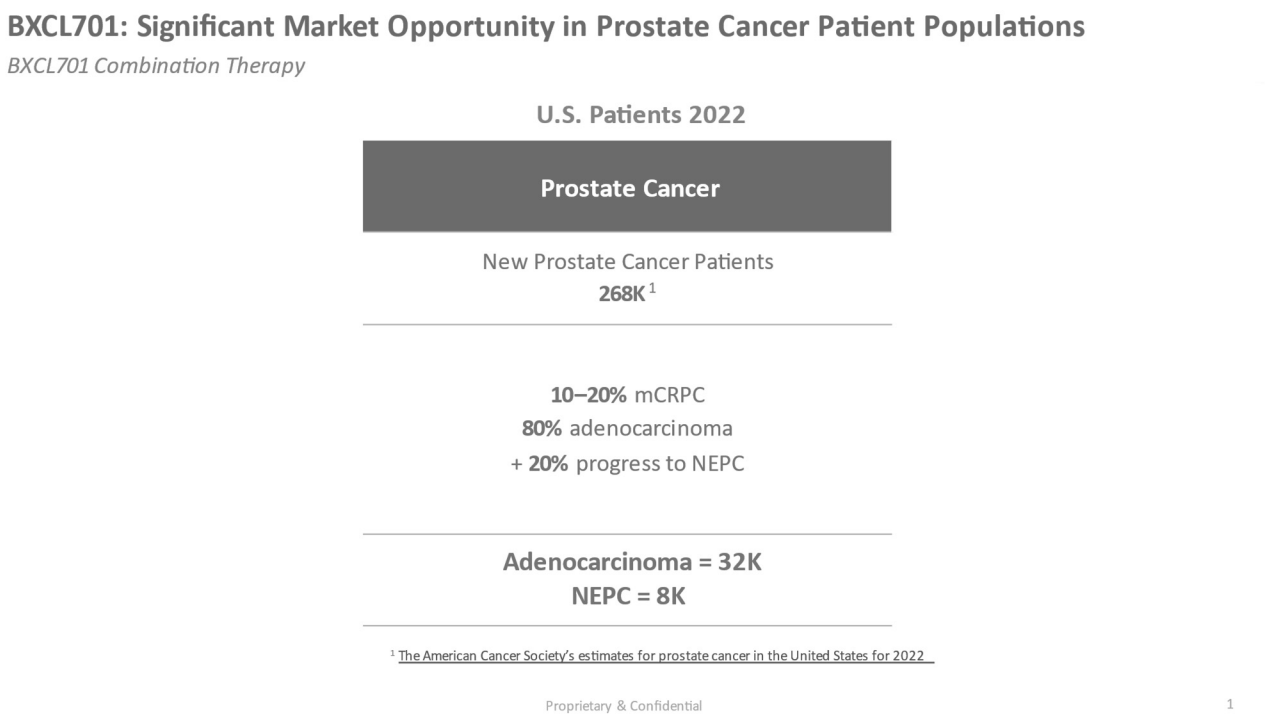
BXCL701 is in development for the treatment of CRPC including the highly aggressive neuro endocrine variant of NEPC, a segment of prostate cancer patients that have progressed on second generation androgen inhibitors (Zytiga® and Xtandi®) . Approximately one in four patients treated with Zytiga and Xtandi are expected to develop NEPC based on current clinical literature. The combined global sales of Zytiga and Xtandi, which are only approved for prostate cancer treatment, were approximately $7 billion in 2020, and we believe such sales number gives a perspective of the potential market for BXCL701 in this indication. Additionally, generic alternatives for Zytiga became available in the U.S. market in 2019, and we, therefore, expect the number of patients with access to androgen inhibitor therapy to increase.

Prostate Cancer Overview and Market Opportunity

Prostate cancer is the most common malignancy and is the second leading cause of cancer death in men in the United States. In 2022, more than 3.1 million men in the United States are living with, or in remission from, prostate cancer. The American Cancer Society's estimates for prostate cancer in the United States for 2022 are about 268,490 new cases of prostate cancer and about 34,500 deaths from prostate cancer. While the five year survival rate of local and regional prostate cancer is almost 100%, more aggressive forms of the disease such as metastatic prostate cancer have a five-year survival rate of approximately 30%. These aggressive forms of prostate cancer can initially be treated with androgen deprivation therapy. However, almost all patients experience a recurrence in tumor growth, which results in the patient having CRPC. An estimated 180,000 men in the United States are eligible for treatment with the second generation anti-androgen drugs Zytiga and Xtandi. These drugs have widely become the standard of care.

Unfortunately, virtually all the patients who respond to Zytiga and Xtandi are expected to progress to even more aggressive forms of prostate cancer requiring further treatment. About one in five of the progressing patients will develop NEPC, for which there is no effective treatment based on information in an article published in the Journal of the National Comprehensive Cancer Network in 2014 by Agarwal et. al. and an article published by Journal of Clinical Oncology in 2014 by Wang et. al. NEPC specifically displays neuroendocrine differentiation, either pathologically with the presence of the typical neuroendocrine small cells, or molecularly by expressing neuroendocrine markers.

The market opportunity for BXCL701 in the initial target markets is detailed below:



Limitations of Current Treatments for CRPC

Despite demonstrated benefit of immunotherapies targeting PD-1—such as pembrolizumab—on clinical outcomes in many solid tumors, mCRPC remains largely resistant to such therapies with single-agent response rates of under 6%. Further exploration has been focused on combination therapies.

There is no approved therapy for NEPC. NEPC patients are treated off-label with cytotoxic chemotherapies, such as platinum-based regimens. These treatments have poor efficacy due to their short duration of response and substantial toxicity. While the immuno-oncology field has made several advances in the treatment of solid tumors, several trials of immuno-oncology agents in patients with prostate cancer, and specifically NEPC, have shown limited or no anti-tumor activity.

BXCL701's potential immunomodulatory mechanism of action may manipulate the tumor micro-environment in such a way to convert a "cold" tumor environment into an inflamed "hot" environment so that prostate cancer can overcome resistance to immunotherapy.

BXCL701 Immuno-Oncology Program

BXCL701 Clinical Trials

BXCL701 is currently being evaluated in two combination therapy clinical trials:

In April 2020, we announced the initiation of the Phase 2 efficacy portion of the Phase 1b/2 trial evaluating BXCL701 in combination with KEYTRUDA® (pembrolizumab, a PD-1 inhibitor) for NEPC. The Phase 1b safety assessment of BXCL701 identified a split dose totaling 0.6 mg per day as the recommended dose when used in combination with KEYTRUDA®. In addition to the efficacy cohort in NEPC patients, in August 2020, we opened a separate cohort for CRPC patients who have failed taxane-based chemotherapy and up to two lines of second-generation androgen pathway blockers. Data from the Phase 1b portion of this trial were presented at the Society for Immunotherapy of Cancer's, or SITC's, 35th Anniversary Annual Meeting in 2020, and an interim efficacy update was presented at ASCO GU Symposium in February 2021. We reported updated interim data from the Phase 2 portion of this trial in NEPC and adenocarcinoma cohort at the ASCO GU Symposium in February 2022. Data from the Phase 2 portion of the trial were previously presented at the European Society for Medical Oncology conference in September 2021 and at ASCO GU in February 2021.

The MD Anderson-led Phase 2 open-label basket trial is designed to evaluate the response rate of orally administered BXCL701, combined with KEYTRUDA, in two arms: Arm A is enrolling checkpoint naïve patients (where checkpoint therapy is indicated: "hot tumors"); and Arm B is enrolling patients who have progressed following checkpoint therapy alone. Interim data were presented at the June 2021 American Society of Clinical Oncology annual meeting. In the first half of 2022, we expect to present additional interim efficacy data from the trial.

Other Immuno-oncology Indications

In addition to CRPC and CPI-refractory tumors, we plan to leverage our existing preclinical and clinical data to identify other cancer types with high unmet medical need that we believe would benefit from BXCL701's novel potential mechanism of action. We are prioritizing indications where the immuno suppressive microenvironment is driven by the potential molecular and cellular targets of BXCL701 and where the single agent activity of approved immune checkpoint inhibitors is limited.

We believe that BXCL701, if successfully developed and approved, may provide a platform for combination with immunotherapy modalities that go beyond the currently approved immune checkpoint agents that target the PD 1/PD L1 axis. Following our proof-of-concept trials, we plan to conduct clinical trials covering a broad range of additional combinations with other immunotherapy agents, including:

- immune checkpoint inhibitors (other than PD-1/PD-L1);

- cellular therapies (CAR-T and chimeric antigen receptor natural killer cells);
- therapeutic vaccines; and
- ADCC driven monoclonal antibodies.

Other Product Candidates

Neuroscience Program

We are targeting neuroscience disorders where there is a high unmet medical need, and therefore, a requirement for symptom management is a priority (such as agitation and symptoms resulting from stress-related behaviors) as well for transformative care for monogenic rare CNS disorders.

For symptomatic approaches, our neuroscience program is developing product candidates with a focus on treating symptoms for various neurological and psychiatric disorders. This entails re innovating existing agents through formulation changes and deuteration. The utilization of our expanding internal AI capabilities along with BioXcel LLC's AI capability has identified several monogenic diseases with available animal models across rare neuroscience diseases. We utilize proprietary algorithms to identify associated mechanisms with existing pharmacology to test whether these agents can improve the disease profile in the animal model either through disease modification or symptomatic manner. The agents identified must be those that we believe are Phase 2 ready with a potential for a short, cost-effective development plan (four to five years to potential NDA submission).

Immuno-oncology Program

Our immuno-oncology program is based on utilizing a comprehensive map of all known relationships that link immuno-evasion and immuno-activation pathways and targets with thousands of pharmacological agents and tumor indications. This comprehensive map has permitted us to select a potential pipeline of candidates based on our ability to alter the tumor micro-environment and the potential to address relevant unmet medical needs for various tumor types.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary products. The immuno-oncology, neuroscience, and rare disease segments of the industry in particular 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 and 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 all 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, are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any medicines we may develop. Our competitors also may obtain FDA or other regulatory approval for their medicines more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. 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. If our therapeutic product candidates are approved, we expect that they 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. If the product candidates of our priority programs are approved for the indications for which we are currently planning clinical trials, they will compete with the drugs discussed below and will likely compete with other drugs currently in development.

Neurological and Psychiatric Disorders

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

Immuno-oncology

The immuno-oncology field is characterized by the rapid evolution of technologies and products and by fierce competition based on the development of compounds, often with similar mechanisms of action. Clinical development plans are further compounded by the possibility of overlapping intellectual property. A wide variety of commercial players, large pharmaceutical companies, established and emerging biotechnology companies, and several not-for-profit entities are actively developing potentially competitive products in immuno-oncology and in our lead indications.

While we believe our product candidates, technology, knowledge, and experience provide us with competitive advantages, we face competition from established and emerging pharmaceutical and biotechnology companies. Such companies include:

- **Major pharmaceutical companies developing multiple immuno-oncology agents:** AstraZeneca PLC, Bristol-Myers Squibb Company, Celgene Corporation, Merck & Co., Inc., Novartis AG, Pfizer Inc., Roche Holding Ltd., and Sanofi SA.

- **Companies developing agents aimed at stimulating the immune response:** AdaptImmune LLC, Idera Pharmaceuticals, Inc., Immune Design Corp., NewLink Genetic Corporation, Advaxis, Inc., Argos Therapeutics, Inc., Biovest International, Inc., ImmunoCellular Therapeutics, Ltd., Immune Design, Inc., Inovio Pharmaceuticals, Inc., Intrexon Corporation and Northwest Biotherapeutics, Inc.

- **Companies developing cell-based immunotherapy approaches:** Intrexon Corporation, Juno Therapeutics, Inc., Kite Pharma, Inc. (acquired by Gilead Sciences, Inc.), Novartis AG and Pfizer Inc.

Manufacturing

We do not have manufacturing facilities. We currently rely on strategic manufacturing partners and expect to continue to rely on third parties for the manufacture of our product candidates for clinical research as well as for eventual, possible commercial manufacturing.

For the supply of drug substance and drug product for our BXCL501 clinical program, we have secured manufacturing partners. We have completed the manufacture of phase III clinical supply and registration batches of our proprietary, sublingual thin film product.

We produce clinical drug product for BXCL701 under exclusivity with the original manufacturers of the active pharmaceutical ingredient, or API, and drug product tablets, respectively.

Manufacturing partners used for both programs currently manufacture commercial products, and we consider them to be suitable for commercial supply for our programs, if approved.

Commercialization

We plan to retain our worldwide commercialization rights for some of our key product candidates, while for other product candidates we could potentially consider collaboration opportunities to maximize returns.

As a Company we have no experience in commercializing products, however, we intend to build our own commercialization organization and capabilities over time. We are considering partnerships, joint ventures, and a variety of business partnerships for the Japanese and European Markets. We currently plan to retain U.S. rights and are working towards a potential BXCL501 approval on April 5, 2022. For example, in the second half of 2021 we fully launched our unbranded disease education campaign to promote awareness around the treatment of agitation in schizophrenia and bipolar disorders. In addition, we fully deployed our Medical Science Liaison and Medical Managed Care teams who actively engaged with healthcare professionals and payors to provide key insights to support our commercial strategy. If BXCL501 is approved outside the United States we would consider launching BXCL501 through collaborations with third parties.

As product candidates advance through our pipeline, our commercial plans may change. Clinical data, the size of the development programs, the size of the target market, the size of a commercial infrastructure, and manufacturing needs may all influence our United States, European Union, and rest-of-world strategies.

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 United States 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, strengthen, and maintain 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.

Patent Portfolio

As of February 1, 2022, our patent portfolio included 6 Patent Cooperation Treaty, or PCT, applications, 16 U.S. utility applications, 1 issued U.S. utility patent, 9 U.S. provisional patent applications, 89 pending non-U.S. applications, 9 allowed or granted non-U.S. patents, 1 design patent application, which is a U.S. design application, and 34 allowed or registered design patents. U.S. Pat. No. 10,792,246, directed to our proprietary sublingual thin-film formulation of Dex, was issued on October 6, 2020 and has a term that is set to expire no earlier than 2039. We plan to list the U.S. patent in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, or Orange Book. We have filed applications in the core patent family protecting BXCL501 in the United States, Taiwan, and other major markets. We expect that patents issuing from these applications, if any, 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 United States, 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 15 countries, including the United States, 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 2037. 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 continue to file new applications on an ongoing basis, including provisional applications directed to treating mania and dementia. If patents issue from those cases, we expect them to expire no earlier than 2041 and 2042, respectively.

We have multiple patent families filed to protect our BXCL701 program, including our core patent family directed to methods of using BXCL701 with immune checkpoint inhibitors, which is filed in the United States and 14 other countries. Any patents issuing from that family should expire no earlier than 2036. We have a PCT application directed to combination therapies using BXCL701 with immune checkpoint inhibitors and approaches for modifying T-cell activity. We expect any patents issuing from this family to expire no earlier than 2038. Additional PCT and ex-US applications are directed to administering BXCL701 in combinations with various other molecules and dosing regimens. We expect that patents issuing from these applications, if any, will expire no earlier than 2039. Finally, we have multiple provisional applications directed to various dosing regimens and combination therapies. Any patents issuing from those applications are expected to expire between 2039 and 2041 at the earliest.

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 United States, 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 United States patent we own or license may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman 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 IND, and the submission date of a 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 the expiration of the patent. The United States Patent and Trademark Office, 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 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 United States. The relevant patent laws and their interpretation outside of the United States are also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our technology or product candidates and enforce the patent rights that we license, and also 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 that are 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 particular 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.

Our Relationship with BioXcel LLC

BioXcel LLC currently holds a 31% interest in the Company and our pipeline compounds have been identified by applying our growing internal AI capabilities along with utilizing BioXcel LLC's expertise in EvolverAI, for drug re-innovation.

We entered into the Amended and Restated Asset 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 Candidates or a product derived therefrom.

We entered into a Separation and Shared Services Agreement with BioXcel LLC that took effect on June 30, 2017, as amended and restated thereafter, or the Services Agreement, pursuant to which services provided by BioXcel LLC through its subsidiaries in India and the United States will continue indefinitely, as agreed upon by the parties. These services are primarily for drug discovery, chemical, manufacturing and controls cost and general and administrative support. Service charges recorded under this agreement were $1.4 million and $1.3 million for the year ended December 31, 2021 and 2020, respectively.

Under the Services Agreement, the Company has an option, exercisable until March 12, 2023, 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. 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 milestones shall not exceed $10 million in the aggregate and not be payable prior to proof of concept in humans and (ii) commercialization milestones 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 September 30, 2024.

We paid $9 million in February 2020 for the purchase and subsequent cancellation of 300,000 shares owned by BioXcel LLC, which is more fully discussed in Note 5 to the financial statements included elsewhere in this Annual Report on Form 10-K.

Government Regulation

Government Regulation and Product Approval

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

U.S. Drug Development Process

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

- completion of preclinical laboratory 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 trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCPs"), to establish the safety and efficacy of the proposed drug for its intended use;
- preparation of and submission to the FDA of an NDA after completion of all pivotal trials;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing 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 of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

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

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed.

Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or 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.

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 investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

In addition, during the development of a drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share

information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the 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 PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the filing date to complete a standard review of an NDA for a drug that is a new molecular entity, 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 reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs.

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

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy ("REMS") to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients

to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, 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 United States

Certain products are comprised of components, such as drug components and device components, that 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 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 a number of expedited development and review programs for qualifying product candidates. For example, the Fast Track program is intended to expedite or facilitate the process for reviewing 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 designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. 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 marketing 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 post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

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

Orphan drug designation and exclusivity

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

If a product that has orphan drug designation subsequently receives the first FDA approval for 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 and a waiver of the NDA application user fee.

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

Post-approval Requirements

Drug products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors 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. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

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

- injunctions or the imposition of civil or criminal penalties.

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

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 Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the 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, also known as 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/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 will apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, if FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, 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 United States, 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, also called 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, PMA approval 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 510(k) marketing clearance, approval of a PMA, 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.

PMA approval 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 approval 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, PMA 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 United States.

International Regulations

In addition to regulations in the United States, 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. Whether or not we obtain FDA approval of 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. 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

Similarly to the U.S., the various phases of non-clinical and clinical research in the European Union ("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 may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be 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 European Medicines Agency ("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 with regard to any future marketing authorization application 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 marketing authorization ("MA"). To obtain regulatory approval of a product candidate in the EU, we must submit a MA application ("MAA"). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" 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/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 MAs" 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 procedure. 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 procedure, 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 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 MA, reference product generally receive 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 United States. 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 procedure. Upon grant of a MA, orphan medicinal products are entitled to ten years of market exclusivity for the approved therapeutic indication. During the ten-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 Norway, Liechtenstein and Iceland.

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 the 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, again, 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 will be subject to further requirements once the in-vitro medical diagnostic devices Regulation (No 2017/746) ("IVDR") will become applicable on 26 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 voted to adopt the proposed regulation on December 15, 2021 and the regulation entered into force on January 2022. The IVDR will fully apply on May 26, 2022 but there will be 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 procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a MAA 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 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 any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any 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.

In 2003, the U.S. government enacted legislation providing a partial prescription drug benefit for Medicare beneficiaries, which became effective at the beginning of 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, to obtain payments under this program, we would be required to sell products to Medicare recipients through prescription drug plans operating pursuant to this legislation. These plans will likely negotiate discounted prices for our products.

Further, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or ACA, was enacted and the Healthcare Reform Law substantially changes the way healthcare is financed in the United States 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 new 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 United States Supreme Court dismissed the judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the United States 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 healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. In addition, we expect that federal, state and local governments in the United States will continue to consider legislation to limit the growth of healthcare costs, including the cost of prescription drugs. Future legislation could limit payments for pharmaceuticals such as the product candidates that we are developing.

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 any 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 United States 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.
In order to raise sufficient financial resources to continue to advance our product candidates, we will need to address pricing pressures and potential third-party reimbursement coverage for our product candidates. In the United States 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.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal, state and foreign laws targeting fraud and abuse in the healthcare industry. Such laws include, without limitation, U.S. federal and state anti-kickback, fraud and abuse, false claims, consumer fraud, data privacy and security, and transparency laws and regulations with respect to drug pricing and payments and other transfers of value made to physicians and other healthcare professionals, as well as similar foreign laws in the 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 healthcare 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 healthcare 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 healthcare 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 healthcare 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 healthcare fraud, and false statements relating to healthcare 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, or 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 healthcare 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 healthcare 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 United States, 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 FTC 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 artificial intelligence and machine learning may be subject to laws and evolving regulations regarding the use of artificial intelligence/machine learning, controlling for data bias, and antidiscrimination.

Human Capital

Our Employees. We have grown to a team of 89 employees as of December 31, 2021, all of whom were employed in the U.S. Our highly qualified and experienced team includes scientists, physicians and professionals across sales,

marketing, manufacturing, regulatory, finance and other important functions that are critical to our success. We also leverage certain experts in drug development employed by BioXcel LLC to provide flexibility for our business needs.

We expect to continue to hire additional employees in 2022 with a focus on expanding our expertise and bandwidth in clinical and preclinical research and development, marketing and sales and finance. We continually evaluate our business needs and opportunities.

Our Culture. 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 sections 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 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 never generated any product revenues, which may make it difficult to evaluate the success of our business to date 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 and advancing the development of, our product candidates, including conducting clinical and preclinical studies. We have not yet demonstrated an ability to successfully obtain marketing approvals, manufacture products on a commercial scale, or arrange for a third party to do so on our behalf or conduct 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 developing and 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 $107.2 million and $82.2 million for the years ended December 31, 2021 and 2020 respectively. As of December 31, 2021, we had stockholders' equity of $221.4 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. None of our product candidates have been approved for marketing in the United States, or in any other jurisdiction, and may never receive such approval. It could be several years, if ever, before we have a commercialized product that generates significant revenues. 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;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;

- hire additional clinical, regulatory, scientific and accounting 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 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 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.

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 of our product candidates. If we are required by the U.S. Food and Drug Administration, or FDA, or other regulatory authorities such as the European Medicines Agency, or 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 BXCL501, BXCL701, BXCL502 and our other product candidates; seek to identify and develop additional product candidates; acquire or in-license other product candidates or technologies; seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any; establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any; 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, 2021 will be sufficient to fund our ongoing research and development efforts and commercialization preparation for at least twelve months from the date of the issuance of the financial statements included in this Annual Report on Form 10-K. We will be required to expend significant funds in order to 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, the net proceeds of our prior equity offerings and 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. Further financing may not be available to us on acceptable terms, or at all. Additionally, market volatility resulting from the COVID-19 pandemic 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.

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 BXCL501, BXCL701, BXCL502 and our other 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 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 as well as establish a commercial infrastructure;
- revenue received from commercial sales, if any, of 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; and
- the costs of operating as a public company.

Risks Related to the Discovery and Development of Product Candidates

We have limited experience in drug discovery and drug development, and we have never had a drug approved.

Prior to the acquisition of our 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 have acquired our product candidates from to have conducted such research and development in accordance with the applicable protocol, legal, regulatory and scientific standards, having accurately reported the results of all clinical trials conducted prior to our acquisition of the applicable product candidate, and having correctly collected and interpreted the data from these studies and trials. To the extent any of these has not occurred, our expected development time and costs may be increased, 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 BXCL501, BXCL701 and BXCL502. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize BXCL501, BXCL701, BXCL502 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 do not have any products that have received regulatory approval and may never be able to develop marketable product candidates. We are investing a significant portion of our efforts and financial resources in the development of BXCL501 and BXCL701, as well as our other product candidates, including BXCL502. 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 BXCL501, BXCL701, BXCL502 and our other product candidates will depend on several factors, including the following:

- acceptance of an IND application by the FDA or acceptance of comparable applications by foreign regulatory authorities allowing us to conduct clinical trials of our product candidates in the United States 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 United States 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 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 as a result 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, and the results and related findings and conclusions 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 were 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 the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Our product candidates 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 a New Drug Application, or NDA, or other submission or to obtain regulatory approval in the United States 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 any of our product candidates. Consequently, we may not have the necessary capabilities, including adequate staffing, to successfully manage the execution and completion of any 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 any of 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, which is currently under review, and have not submitted any similar marketing applications to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations. Even if we successfully obtain 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 our product candidates are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our product candidates both in the United States, 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 Clinical Trials Regulation, or 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 clinical trial application, or 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 may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be 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, or 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 healthcare resources to combat epidemics, such as the COVID-19 pandemic;
- obtaining institutional review board, or IRB, approval at each site, or independent ethics committee, or IEC, approval at any sites outside the United States;
- 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 serious adverse events 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 good manufacturing practice, or 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, good clinical practice, or 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 the ICU settings, including as a result of the burden COVID-19 has placed on the ICU.

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, or 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 as a result of differences in healthcare 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 in order for us 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, the proximity of patients to study sites, 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 may be impacted by governmental restrictions and diversion of healthcare resources resulting from the COVID-19 pandemic. Many pharmaceutical companies are conducting clinical trials in patients with the disease indications that our potential drug products 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, if any.

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, BXCL701, BXCL502 and our other product candidates in patients, in many cases, is still in the early stages 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. In such an event, 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 for our clinical trials and upon any commercialization of any of our product candidates. 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 one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, 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 Risk Evaluation and Mitigation Strategies, or 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 candidate or for particular indications of a 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 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 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 both novel and unproven. Because our approach is both novel and unproven, 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 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 product candidates for clinical development or 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 have obtained Fast Track designation for BXCL501 for the acute treatment of mild-to-moderate agitation associated with schizophrenia, bipolar disorder, or 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 have obtained Fast Track designation for BXCL501 for the acute treatment mild-to-moderate agitation associated with schizophrenia, bipolar disorder, or dementia, and we may seek Fast Track designation for other indications for BXCL701 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 have 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 time 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, including BXCL501. The Hatch-Waxman Act added Section 505(b)(2) to the Federal Food, Drug and Cosmetic Act, or 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 BXCL501. 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 (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 In Vitro Medical Devices Regulation (No 2017/746) or 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 will only become applicable 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 will fully apply on May 26, 2022 but there will be 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 as of the entry into force of the IVDR which 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 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.

Even if we obtain regulatory approval for BXCL501, BXCL701, BXCL502 or any product candidate, we will still face extensive and ongoing regulatory requirements and obligations and any product candidates, if approved, may face future development and regulatory difficulties.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising and promotional activities for such product, among other things, will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements,

continued compliance with cGMP or similar foreign requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval.

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product candidate may be marketed or to the conditions of approval, including a requirement to implement a REMS or similar risk management measures. If any of our product candidates receives marketing approval, the accompanying label may limit the approved indicated use of the product candidate, which could limit sales of the product candidate. The FDA or foreign regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. Violations of the FDCA or similar foreign regulations relating to the promotion of prescription drugs may lead to FDA or foreign regulatory authority enforcement actions and investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events 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 United States or abroad.

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

If we are found to have improperly promoted off-label uses of our products or product candidates, if approved, we may become subject to significant liability. Such enforcement has become more common in the industry. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for our product candidates for our proposed indications, physicians may nevertheless use our products for their patients in a manner that is inconsistent with the approved label, if the physicians personally believe in their professional medical judgment it could be used in such manner. However, 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 request 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 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. 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, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. More recently, 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. Regulatory authorities outside the United States 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, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite 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 which may 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 United States and may not obtain marketing approvals for products in Europe and other jurisdictions.

In addition to regulations in the United States, should we or our collaborators pursue marketing approvals for BXCL501, BXCL701, BXCL502 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 BXCL501, BXCL701, BXCL502 and our other product candidates in Europe and other jurisdictions outside the United States 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 United States regulatory and 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 United Kingdom, or 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, however 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 GMP, inspections of manufacturing facilities for medicinal products and GMP 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, or MHRA, launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closes on 14 March 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 marketing authorizations (Northern Ireland is covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). As of 1 January 2021, all existing centralized marketing authorizations were automatically converted into UK marketing authorizations effective in Great Britain and issued with a United Kingdom marketing authorization number on January 1, 2021 (unless marketing authorization holders opted out of this scheme). A separate marketing authorization 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 marketing authorization applications 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 the 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 marketing authorization, 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 marketing authorization and commercialization of products in the EU and/or the UK.

If we are found in violation of federal, state or foreign "fraud and abuse" laws, we may be required to pay a penalty and/or be suspended from participation in federal or state health care programs, which may adversely affect our business, financial condition and results of operations.

In the United States, we will be 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, particularly upon successful commercialization of our products in the United States. We may have to comply with similar laws and regulations outside the United States. 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;

- the Health Insurance Portability and Accountability Act of 1996, or 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 healthcare 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 healthcare program, unless an exception applies;

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

- the federal physician sunshine requirements under the ACA, which requires certain manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or 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 other healthcare providers 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 healthcare 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 healthcare providers or marketing expenditures and pricing information; and; and

- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare 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 healthcare 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, and imprisonment, 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 is in excess of the limits of our insurance coverage. We expect we will supplement our clinical trial coverage with product liability coverage in connection with the commercial launch of BXCL501, BXCL701, BXCL502 or other product candidates we develop in the future; however, 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 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 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 have been granted 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 United States 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 United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. 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 application for marketing authorization.

In the United States, 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 for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same disease or condition for seven years, except in limited circumstances the applicable exclusivity period is ten 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 indications or for our 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 United States 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 moieties 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 moiety 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 time or regulatory review time of a drug nor gives the drug any advantage in the regulatory

review or approval process, nor does it 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 BXCL501, BXCL701, BXCL502 or any other product candidate.

We have no experience in marketing and selling drug products. We have not entered into arrangements for the sale and marketing of BXCL501, BXCL701, BXCL502 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 this 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. If we seek to market and sell our drugs directly, we will need to hire additional personnel skilled in marketing and sales. 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 establishment of a direct sales force or a contract sales force or a combination direct and contract sales force to market our products will be expensive and time-consuming and could delay any product launch. Further, we can give no assurances that we may 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 United States, 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 in order 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 any product candidate we commercialize, if any. The inability to compete with existing or subsequently introduced drugs would harm our business, financial condition and results of operations.

Even if we obtain regulatory approvals to commercialize BXCL501, BXCL701, BXCL502 or our other product candidates, our product candidates may not be accepted by physicians or the medical community in general.

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

- our demonstration of the clinical efficacy and safety of BXCL501, BXCL701, BXCL502 and our other product candidates;
- timing of market approval and commercial launch of BXCL501, BXCL701, BXCL502 and our other product candidates;
- the clinical indication(s) for which BXCL501, BXCL701, BXCL502 and our other product candidates are approved;
- product label and package insert requirements;
- advantages and disadvantages of our 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 reimbursement codes and coverage in select jurisdictions, and future changes to reimbursement policies of government and third-party payors.

Significant uncertainty exists as to the coverage and reimbursement status of any product candidate for which we obtain regulatory approval. In the United States and markets in other countries, sales of any 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.

Other 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. Our proposed products 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 and state proposals and health care reforms are likely which could limit the prices that can be charged for the product candidates that we develop and may further limit our commercial opportunities. Our results of operations could be materially adversely affected by proposed healthcare reforms, by the Medicare prescription drug coverage legislation, 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.

In September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-marketing authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluations and mitigation strategies approved by the FDA. The FDA's exercise of this authority could result in delays or increased costs during product development,

clinical trials and regulatory review, increased costs to assure compliance with post-approval regulatory requirements, and potential restrictions on the sale and/or distribution of approved products.

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

The U.S. government and other governments have shown significant interest in pursuing healthcare reform. Any government-adopted reform measures could adversely impact the pricing of healthcare products and services in the United States 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 healthcare 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 United States, new healthcare legislation or fiscal challenges faced by government health administration authorities. Specifically, in both the United States 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, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the ACA, has substantially changed the way healthcare is financed by both government health plans and private insurers, and significantly impacts the pharmaceutical industry. The ACA contained a number of provisions that are expected to impact our business and operations in ways that may negatively affect our potential revenues in the future. For example, the ACA imposed a non-deductible excise tax on pharmaceutical manufacturers or importers that sell branded prescription drugs to government programs which we believe will increase the cost of our products. 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 now required to provide a discount on branded prescription drugs equal to 70% of the government-negotiated price, 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 significant changes to the 340B drug discount program including expansion of the list of eligible covered entities that may purchase drugs under the program. At the same time, the expansion in eligibility for health insurance benefits created under ACA is expected to increase the number of patients with insurance coverage who may receive our products.

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 healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes include the Budget Control Act of 2011, which resulted in aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken, as well as the American Taxpayer Relief Act of 2012, which, among other things, 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.

Recently, there has also been heightened government 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 to, among other things, reform government program reimbursement methodologies. Individual states in the United States have also become increasingly active in passing legislation and 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, designed 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.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare 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 the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any 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.

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, 2021, BioXcel LLC owned approximately 31% of the economic interest and voting power of our outstanding common stock. Drs. Mehta and 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." Even though BioXcel 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 Separation and Shared Services Agreement and the Amended and Restated Asset Contribution Agreement, or the Contribution Agreement, that we have entered into with BioXcel LLC have not been negotiated on behalf of BioXcel LLC by persons consisting solely of disinterested BioXcel LLC directors.

No assurance can be given that any stockholder of BioXcel LLC will not claim in a lawsuit that such terms in fact are not in the best interests of BioXcel LLC and its stockholders, that the directors and officers of BioXcel LLC breached their fiduciary duties in connection with such agreements and that any disclosures by BioXcel LLC 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 will 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. The Company has 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, the Company has an option, exercisable until March 12, 2023, 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. 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 milestones shall not exceed $10 million in the aggregate and not be payable prior to proof of concept in humans and (ii) commercialization milestones 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 September 30, 2024. In addition, BioXcel LLC has granted us 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. This option for first negotiation shall be valid for a period of five years from the date of our IPO. If our rights and access to BioXcel LLC's collaborative services and to its EvolverAI were to become limited, terminated, or if we were otherwise precluded from conducting research and development using its 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 except for remedies available to us under our agreements with BioXcel LLC, we cannot control whether or not 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. In addition, if we fail to comply with our diligence, payment or other obligations under the agreements, any such collaboration may terminate or we may not be able to successfully negotiate agreements for future product candidates or collaborations with BioXcel LLC.

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, each of 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., is a manager of BioXcel LLC, as well as a director, officer and stockholder of BioXcel LLC, BTI's former parent company. Additionally, as of December 31, 2021, each of Dr. Mehta and Dr. Nandabalan, through their beneficial ownership of BioXcel LLC, beneficially owned approximately 32% and 32%, 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, 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;
- 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 its 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, biotech, 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 its 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 its 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 we intend to rely on third parties to produce commercial supplies of any 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.

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 all of the manufacturers that we intend to use must adhere to the cGMP or similar foreign regulations prescribed by the FDA or foreign regulatory authorities.

We expect therefore to rely on third-party manufacturers for clinical supplies of our product candidates that we may develop. These third-party manufacturers will be required to comply with cGMPs, and other applicable laws and regulations. We will 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 and/or our 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 or our 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 may be affected, which could disrupt their activities and, as a result, we could face difficulty sourcing key components necessary to produce supply of our 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, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.

In order to conduct clinical trials of our product candidates and commercialize any approved product candidates, we, or our manufacturers, 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 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 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 product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our 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 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 any future 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 European Economic Area ("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 or not 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 GLP 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 additional 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.

In 2020, the novel coronavirus disease, COVID-19, was declared a pandemic and spread across the globe, including throughout the United States and Europe. The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. We have taken steps to protect our workforce and have instituted strict work rules to protect our employees. Beginning late in the first quarter of 2021, and in line with State of Connecticut guidelines, we opened our office on a voluntary basis up to full capacity. In May 2021, the State of Connecticut lifted all business and office restrictions in the State. We have instituted a return to the office policy and will continue to evaluate that policy over the next several months.

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 healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, 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 outbreak impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as rate of infection, the duration of the pandemic and subsequent waves of infection, the prevalence of new variants of the virus, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, the availability, adoption and effectiveness of any vaccines or treatments and the effectiveness of actions taken in the United States and other countries to contain and address the disease. 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 entered into 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, operational, technical and scientific, financial and other resources in order to manage our operations and clinical trials, establish independent manufacturing, continue our research and development activities, and commercialize our product candidate. 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 BXCL501, BXCL701, BXCL502 and our other product candidates;

- manage our internal development efforts effectively while carrying out our contractual obligations to licensors, contractors and other third parties;

- continue to improve our operational, financial and management controls and reporting systems and procedures; and

- attract and retain sufficient numbers of talented employees.

We may utilize the services of third-party vendors to perform tasks including pre-clinical 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 general and administrative functions. We have been relying on our commercial readiness team in connection with the potential commercialization of BXCL501. 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. For example, we are continuing to build our commercial readiness team following the departure of certain senior executives. 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 in the past experienced, and we expect to continue to experience in the future, difficulty in hiring and retaining highly skilled personnel with appropriate qualifications or experienced increased costs to recruit such personnel. The pool of qualified personnel with experience working with the pharma 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 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 healthcare

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 healthcare 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 in the course of 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 to manufacture BXCL501 and BXCL701 and 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, 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 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 could occur through a variety of methods such as cyber-attacks or cyber-intrusions over the Internet, malware, computer viruses, email spoofing, attachments to e-mails, persons inside our organization, 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 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 artificial intelligence and machine learning may be subject to laws and evolving regulations regarding the use of artificial intelligence/machine learning, controlling for data bias, and antidiscrimination. 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. 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 is expected to increase 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. Further, the CPRA recently passed in California, which will impose 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 will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In the event that 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 General Data Protection Regulation, or 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 United States, and the efficacy and longevity of current transfer mechanisms between the EU and the United States remains uncertain. For example, in 2016, the EU and United States agreed to a transfer framework for data transferred from the EU to the United States, called the Privacy Shield, but the Privacy Shield was invalidated in July 2020 by the Court of Justice of the EU, or CJEU. The European Commission issued revised standard contractual clauses, or SCCs, on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the UK; the UK's Information Commissioner's Office launched a public consultation on its draft revised data transfers mechanisms in August 2021. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses 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 have 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 £17.5 million or 4% of global turnover. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/ extends that decision, and remains under review by the Commission during this period. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the UK will be regulated in the long term. These changes may lead to additional costs and increase our overall risk exposure.

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.

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 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 may be limited.

At December 31, 2021, the Company had federal net operating loss carryforwards, or NOLs, of approximately $139 million and state NOLs of approximately $139 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 taxable years beginning after December 31, 2020. As of December 31, 2021, we also had approximately $6.5 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, or the Code, 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 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 United States and in certain foreign jurisdictions. Patents issue from non-provisional applications, which are typically filed from provisional patent applications or from Patent Cooperation Treaty (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. As of February 22, 2022, we had 7 allowed or issued foreign patents relevant to our BXCL701 program and 1 issued U.S. utility patent, 1 pending U.S. design patent application, 4 allowed or issued foreign patents and 34 issued foreign design patents relevant to our BXCL501 program. 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 United States or in foreign jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States 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 U.S. Patent and Trademark Office, or 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 a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include 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 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.

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 Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, apply. In accordance with the Hatch-Waxman Act, such NDAs may be required to include certifications, known as paragraph IV certifications, that certify that any patents listed in the Patent and Exclusivity Information Addendum of the FDA's publication, Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the 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 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, or NCE, 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 United States, 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 United States may be maintained in secrecy until the patents are issued;
- patent applications in the United States 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 US patent applications on inventions similar to ours that claims 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 United States. 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 and BXCL701, 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 significantly 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 United States; 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, AIA or Leahy-Smith 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 U.S. Patent and Trademark Office, 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”;
- 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, 2021, 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, or 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 either of those sections of 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 small 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, or 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, 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 the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

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, 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 results in a decline in the market price of our common stock.

Our certificate of incorporation and 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 and 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 10,000,000 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 and the Notes. 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 United States 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 additional legal, accounting and other expenses that we did not incur as a privately held subsidiary of BioXcel LLC. The obligations of being a public company in the United States 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 of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank 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." In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage that we had through BioXcel LLC. 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 of 2002 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 in significant 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 February 20, 2022, there were 10 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.

Sales of Unregistered Sales of Securities

None.

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.

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 "Selected Financial Data" and our 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

We are a clinical stage biopharmaceutical company utilizing artificial intelligence approaches to develop transformative medicines in neuroscience and immuno-oncology. Our drug re-innovation approach leverages existing approved drugs and/or clinically validated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indices. We believe that this differentiated approach has the potential to reduce the cost and time of drug development in diseases with a substantial unmet medical need.

Our two most advanced clinical development programs are BXCL501, a proprietary, orally dissolving, sublingual thin film formulation of the adrenergic receptor agonist dexmedetomidine ("Dex"), for the treatment of agitation resulting from neuropsychiatric disorders, and BXCL701, 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.

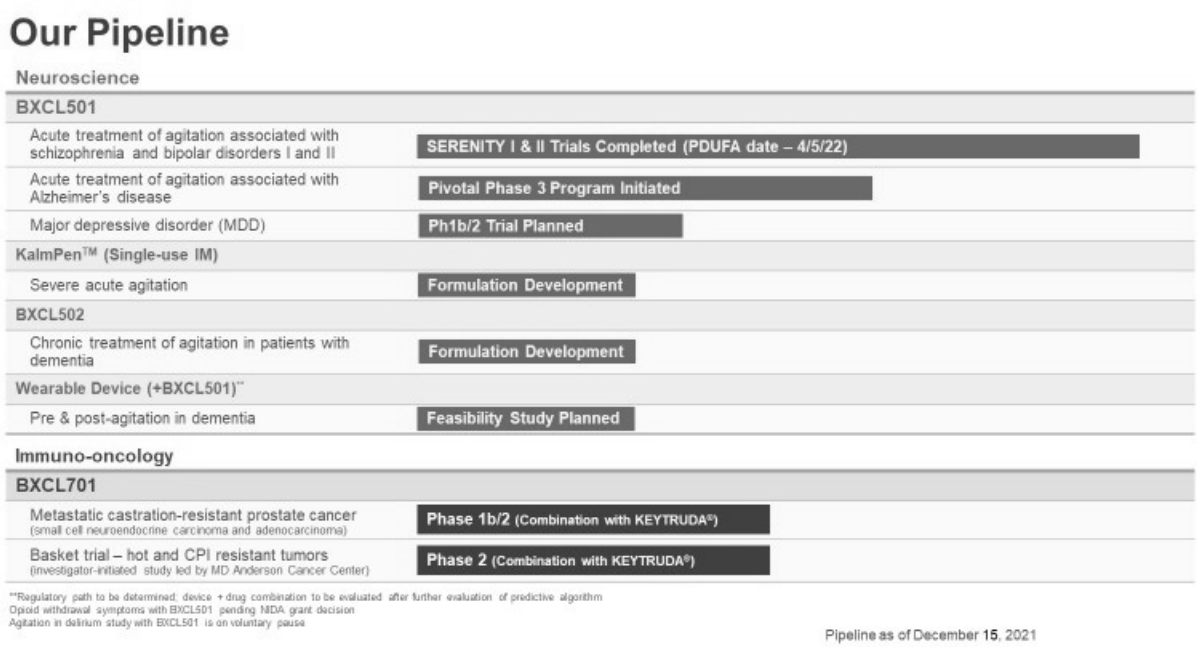
During the first quarter ended March 31, 2020, and continuing through December 31, 2021, COVID-19 was declared a pandemic and spread to multiple regions across the globe, including the United States and Europe. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen.

To date, we have taken steps in line with guidance from the U.S. Centers for Disease Control and Prevention ("CDC") and the State of Connecticut to protect the health and safety of our employees and the community. In particular, we implemented a work-from-home policy for all employees and have restricted on-site activities to certain chemical, manufacturing and control ("CMC") and clinical trial activities. We continue to assess the impact of the COVID-19 pandemic to best mitigate risk and continue the operations of our business. Beginning late in the second quarter of 2020, we began to slowly bring our staff, in very limited numbers, back to our office. This modified return-to-work approach is continuing into 2022. We have taken steps to protect our workforce and have instituted strict work rules to protect our employees.

We continue to work closely with our clinical sites to monitor the potential impact of the evolving COVID-19 pandemic. We remain committed to our clinical programs and development plans. Other than our Phase 2 clinical trial evaluating BXCL501 in patients with delirium through December 31, 2021, we have not experienced any significant delays to our ongoing or planned clinical trials, except for challenges in accessing elderly care facilities and ICU settings; however, this could rapidly change.

Our Clinical Programs

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



Our Novel Drug Re-Innovation Approach

We are developing and implementing holistically throughout the drug development process an artificial intelligence ("AI") eco system designed to rapidly identify drugs that engage novel targets related to indications in psychiatric and neurological rare diseases. In addition, we focus our development on those indications related to or caused by stress. This capability complements our existing work done with BioXcel LLC's EvolverAI and the clinical development group by providing a rich source of new previously unexplored opportunities. 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 lone agents. New combinations of drugs provide the opportunity to evaluate lower, potentially safer doses of drugs and also provide the basis for stronger intellectual property positions. The AI team works closely with business development 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 pharma company pipelines that are 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, 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 identifying combinations that we believe may have a higher probability of success.

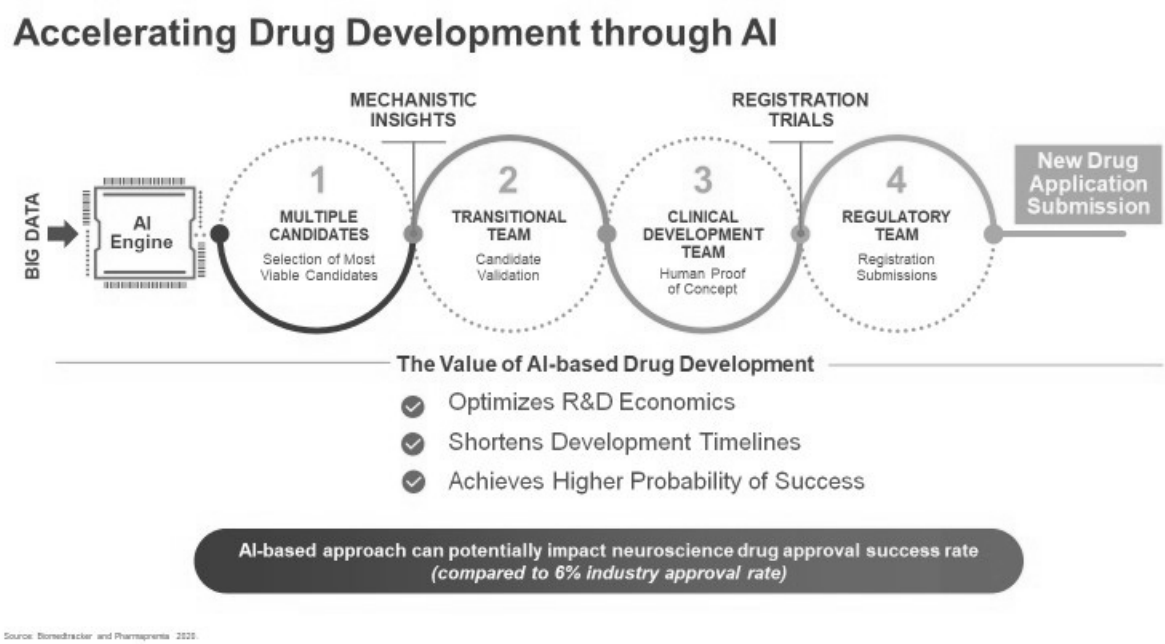
Traditional drug development is plagued with low success rates (13.8%, according to an MIT study of 186,000 trials from January 2000 to October 2015), long drug development cycles (10-15 years, according to PhRMA Key Facts 2016), and exorbitant development costs ($2.6 billion per drug, according to PhRMA Key Facts). Furthermore, many

serious diseases continue to go unaddressed due to limitations of the current drug discovery paradigm. The pharmacological space spans more than 27,000 active pharmaceutical agents, and 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 need and recoupment of 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. They 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 sacrificing 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 prioritizes those compounds with structural design features that may contribute to high blood-brain barrier permeability, which may increase the likelihood of compound brain penetration. Lack of brain penetration is a common cause for failure of many drugs developed for neuropsychiatric indications. We are prioritizing compounds with available human safety data, acceptable pharmacokinetic results, and data that support 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 of 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 150 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 our therapeutic area expertise and our ability to generate therapeutic candidates in neuroscience and immuno oncology through our exclusive collaborative relationship in those areas with BioXcel LLC gives us a significant competitive advantage.

Our approach is illustrated below:



Source: Biomedtracker and Pharmaprenia 2020.

Basis of Presentation

The Company's financial statements are prepared in accordance with Generally Accepted Accounting Principles in the United States of America ("GAAP"). All amounts are presented in thousands.

Components of Our Results of Operations

Revenues

We have not recognized any revenue since inception.

Operating Costs and Expenses

Research and Development

Our research and development expenses reflect costs incurred for the research and development of our clinical and pre-clinical product candidates, which includes payments to BioXcel LLC. Research and development expense 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 ("CROs") and sites that conduct our non-clinical studies and clinical trials, costs of outside consultants engaged in research and development activities, including their fees, stock-based compensation and travel expenses, the cost of acquiring, developing and manufacturing pre-clinical and clinical trial materials and lab supplies, and depreciation and other expenses.

We expense research and development costs to operations as incurred.

Our research and development costs by program for the years ended December 31, 2021 and 2020 are as follows:

	Year Ended December 31,	
	2021	2020
Direct external costs		
BXCL501	$ 16,046	$ 34,430
BXCL701	11,092	7,747
Other research and development programs	1,587	896
Total direct external costs	28,725	43,073
Internal personnel costs	21,282	13,700
Sub-total direct costs	50,007	56,773
Indirect costs and overhead	3,063	1,765
Research and development tax credit	(362)	(543)
Total research and development expenses	$ 52,708	$ 57,995

General and Administrative

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

We expect that our general and administrative expenses will increase as we expand our clinical programs. We also expect increased administrative costs resulting from our clinical trials and the potential commercialization of our product candidates. We believe that these increases will likely include increased costs for director and officer liability insurance, hiring additional personnel to support future market research and future product commercialization efforts and 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.

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 financial statements included in this Annual Report on Form 10-K.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

Revenues

We have not recognized any revenues since inception.

Research and Development Expense

Research and development expenses for the years ended December 31, 2021 and 2020 were $52,708 and $57,995, respectively. Research and development expenses for the years ended December 31, 2021 and 2020 were comprised as follows:

	Year Ended December 31,			
	2021	2020	Change	% Change
Personnel and related costs	$ 14,624	$ 8,408	$ 6,216	74 %
Non-cash stock-based compensation	6,658	6,020	638	11 %
Professional fees	11,932	7,106	4,826	68 %
Clinical trials expense	14,226	30,808	(16,582)	(54)%
Chemical, manufacturing and controls cost ("CMC")	3,506	5,109	(1,603)	(31)%
Travel and other costs	2,124	1,087	1,037	95 %
Research and development tax credit	(362)	(543)	181	33 %
Total research and development expenses	$ 52,708	$ 57,995	$ (5,287)	(9)%

The decrease of $5,287 for the year ended December 31, 2021 is primarily attributable to:

Decreased Clinical trial expenses resulting from the completion of our SERENITY I and II, TRANQUILITY, RELEASE and BXCL501 bioavailability clinical trials, partially offset by increased costs related to the 40mcg cohort expansion of our Tranquility trial. These decreases were further offset by increased costs in our BXCL701 prostate cancer and basket trials.

Lower CMC costs tracked the decrease in fewer BXCL501 manufacturing costs.

The decreases were partially offset by:

Increased personnel and related costs due to our efforts to enlarge our clinical and medical teams as we expanded our clinical and medical programs during the year in preparation of the potential commercial launch of BXCL501 in the U.S.

Increased non-cash stock-based compensation as result of the additional personnel hired during the year. However, the increase was moderated by a combination of reduced expense due to forfeitures and lower grant date fair values resulting from lower market prices of the Company’s common stock.

The increase in professional fees was generally due to increased regulatory, consulting and toxicology fees related to the BXCL501 program.

Travel and other costs were higher due to increased headcount.

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 program provides for such exchange of the research and development credit at a rate of 65% of the annual research and development credit. The benefit for such exchange is recorded as a reduction of research and development expenditures. The credit decreased in 2021 as a result of lower clinical trial activity.

General and Administrative Expense

General and administrative expenses for the years ended December 31, 2021 and 2020 were $54,227 and $24,302, respectively. General and administrative expenses for the years ended December 31, 2021 and 2020 were comprised as follows:

	Year Ended December 31,			
	2021	2020	Change	% Change
Personnel and related costs	$ 9,576	$ 3,422	$ 6,154	180 %
Non-cash stock-based compensation	12,798	8,591	4,207	49 %
Professional fees	10,647	5,473	5,174	95 %
Commercial	16,070	2,487	13,583	546 %
Insurance	2,136	1,611	525	33 %
Travel and other costs	3,000	2,718	282	10 %
Total general and administrative expenses	$ 54,227	$ 24,302	$ 29,925	123 %

The increase of $29,925 for the year ended December 31, 2021 is primarily attributable to:

Increased personnel and related costs due to substantially higher headcount in 2021 in preparation of the potential commercial launch of BXCL501 in the U.S.

Increased non-cash stock-based compensation as result of the granting of awards to increased number of personnel hired during the year. However, the increase was moderated by a combination of reduced expense due to forfeitures and lower grant date fair values resulting from lower market prices of the Company's common stock.

Increased professional fees due to the expanding growth of our operations and was primarily related to increased corporate patent legal fee and investor relations fees.

Significant commercial costs incurred due to the increased complexity and growth as we prepare for the potential commercial launch of BXCL501 in the U.S. We also experienced increased market research fees related to the potential commercial launch of BXCL501 in the U.S.

Increased insurance costs primarily related to an increase in Director and Officer liability premiums.

Travel and other expenses approximated the prior year.

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.

Liquidity and Capital Resources

As of December 31, 2021, we had cash and cash equivalents of $232,968, working capital of $220,145 and stockholders' equity of $221,667. Net cash used in operating activities was $82,153 and $66,350 for the years ended December 31, 2021 and 2020, respectively. We incurred losses of approximately $106,931 and $82,169 for the years ended December 31, 2021 and 2020, respectively. We have not yet generated any revenues and we have not yet achieved profitability. We expect that our research and development and 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 existing cash and cash equivalents as of December 31, 2021 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, 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 in light of the economic downturn and ongoing uncertainty related to the COVID-19 pandemic. If we are unable to secure adequate additional funding as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more product candidates. In addition, the magnitude and duration of the COVID-19 pandemic and its impact on our liquidity and future funding requirements is uncertain as of the filing date of this Annual Report on Form 10-K, as the pandemic continues to evolve globally. See "Risk Factors—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." in Part I, Item 1A. of this Annual Report on Form 10-K for a further discussion of the potential impact of the COVID-19 pandemic on our business.

Sources of Liquidity

We have focused our efforts on raising capital and building the products in our pipeline. Since our inception, our operations have been financed primarily by BioXcel LLC and from proceeds from the sale of equity securities, including stock issuances including our initial public offering, private placements of our common stock, and registered offerings of our common stock and an Open Market Sale Agreement ("ATM Program"). 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 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, par value $0.001 per share (the "Common Stock"), having an aggregate offering price of up to $100,000, from time to time, through an "at the marketing 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.

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 February 2020, we sold in a registered offering 2,300 shares of our common stock at a public offering price of $32.00 per share for gross proceeds of $73,600 less underwriting discounts and commissions. We received net proceeds of approximately $68,811.

We received funds under the Paycheck Protection Program of the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") in April 2020 in the amount of $537. On April 23, 2020 the Small Business Administration issued a new FAQ #31, which provided guidance on what it means to certify that: "current economic uncertainty makes this loan request necessary to support the ongoing operations of the Applicant." Following review of this new FAQ #31 we decided to withdraw from the Paycheck Protection Program and have repaid the loan in full together with all accrued interest.

In July 2020, we sold in a registered offering 4,000 shares of our common stock at a public offering price of $50.00 per share for gross proceeds of $200,000 less underwriting discounts and commissions. We received net proceeds of approximately $186,974.

Cash Flows

(in thousands)	Year Ended December 31, 2021	2020
Cash provided by (used in)		
Operating activities	$ (82,153)	$ (66,350)
Investing activities	(445)	(316)
Financing activities	102,447	247,359

Operating Activities

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 $130 increase 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.

Cash used in operating activities was $66,350 for the year ended December 31, 2020 and was primarily attributable to our $82,169 net loss and a $2,301 increase in prepaid expenses and other assets, partially offset by $14,611 in stock-based compensation and a $3,197 increase in accounts payable, accrued expenses and other liabilities.

Investing Activities

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.

Cash used in investing activities was $316 for the year ended December 31, 2020 and was attributable to the purchase of equipment and leasehold improvements.

Financing Activities

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, and $4,056 in net proceeds from the sale of common stock under our ATM Program. Proceeds of $1,454 from the exercise of stock options provided the remainder.

Net cash provided by financing activities was $247,359 for the year ended December 31, 2020 and was primarily attributable to the net proceeds of $68,811 from our February 2020 offering combined with net proceeds of $186,974 from our July 2020 offering. Additionally, we received $598 in proceeds from the exercise of stock options. This amount was partially offset by $9,024 used for the purchase and cancellation of 300,000 shares of common stock owned by BioXcel LLC in February 2020.

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 expand our clinical trials of BXCL501 and BXCL701, seek marketing approval for our product candidates and pursue development of our other product candidates. We do not expect to generate revenue unless and until we successfully complete development and obtain regulatory approval for our product candidates. 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 BXCL501 and BXCL701;
- conduct additional research and development with our product candidates;
- seek to identify, acquire, license, develop and commercialize additional 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 efforts;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize 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, 2021 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 financial statements included in this Annual Report on Form 10-K and will be sufficient to fund our ongoing research and development efforts and commercialization preparation through 2022. We expect that we will need to obtain substantial additional funding in order to fund our 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, that 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 BXCL501, BXCL701 or other 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 BXCL501, BXCL701 or other product candidates that we otherwise would seek to develop or commercialize ourselves.

Critical Accounting Policies and Estimates

The preparation of our financial statements in conformity with 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 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.

A description of significant accounting policies that require us to make estimates and assumptions in the preparation of our financial statements is as follows:

Stock-based Compensation

The Company accounts for stock-based compensation in accordance with ASC 718, "*Compensation—Stock Compensation,*" which requires the measurement and recognition of compensation expense based on estimated fair market values for all share-based awards made to employees and non-employee service providers, including stock options. 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 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.

The Company's stock option awards are valued at fair value on the date of grant and that fair value is recognized over the requisite service period. The Company utilizes the Black-Scholes option pricing model for determining the estimated fair value for stock-based awards. The Black-Scholes model requires the use of assumptions which determine the fair value of the stock-based awards. Determining the fair value of stock-based awards at the grant date requires judgment, including estimating the expected term of the stock options, the expected volatility of our stock and expected dividends. Prior to the IPO, significant judgement and estimates were used to estimate the fair value of these awards, as the shares of common stock underlying these awards were not then publicly traded. Stock awards granted by the Company subsequent to its IPO are valued using market prices at the date of grant. The Company has elected to account for forfeitures as they occur, by reversing compensation cost when the award is forfeited.

Research and Development Accruals

Research and development costs are expensed as incurred. Clinical study costs are accrued over the service periods specified in the contracts and adjusted as necessary based upon an ongoing review of the level of effort and costs actually incurred. The Company's assessment of the completeness of the information is subject to variability and uncertainty. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In addition, in certain circumstances, the determination of the nature and amount of services that have been received during the reporting period requires judgment as the timing and pattern of vendor invoicing does not correspond to the level of services provided. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly.

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.

Income Taxes

We use 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.

We apply the provisions of ASC 740, Income Taxes, which 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. Our financial statements reflect expected future tax consequences of such positions presuming the taxing authorities' full knowledge of the position and all relevant facts.

We do not have any unrecognized tax benefits as of December 31, 2021. We review 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.

Contractual Obligations and Commitments

In August 2018, the Company entered into an agreement to lease approximately 11,040 square feet of space on the 12th floor of the building located at 555 Long Wharf Drive, New Haven, Connecticut (the "12th Floor Lease) which was effective February 22, 2019. The 12th Floor Lease expires in February 2026.

In August 2020, the Company entered into an amendment to the 12th Floor Lease wherein the Company leased an additional 7,245 square feet of space on the 12th floor of the building located at 555 Long Wharf Drive, New Haven, Connecticut (the "12th Floor Lease Amendment"). The 12th Floor Lease Amendment expires in February 2026.

The following table summarizes our contractual obligations related our 12th Floor Lease and the 12th Floor Lease Amendment at December 31, 2021 and the effect such obligations are expected to have on our liquidity and cash flow in future periods:

	Payments due by Period				
	Total	Less Than 1 year	1-3 years	3-5 years	More Than 5 years
Operating lease commitments	$ 1,572	$ 363	$ 753	$ 456	$ —

For additional details, see "Note 10 to Financial Statements – Leases."

Off-Balance Sheet Arrangements

We did not have any off-balance sheet arrangements as of December 31, 2021 or 2020, as defined under SEC rules.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk. As of December 31, 2021, we had $232,968 cash and cash equivalents. Our cash equivalents are primarily held in U.S. Government money market funds. We do not participate in any foreign currency hedging activities and we do not have any other derivative financial instruments. We did not recognize any significant exchange rate losses during the years ended December 31, 2021 and 2020, 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 does not contain excessive 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 are in excess of federally insured limits.

Capital Market Risk. We currently have no product revenues and depend on funds raised through other sources. Our sources of funding include 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 reports of our independent auditor and our former independent auditor are presented beginning on page F-1 and are incorporated under this Item by reference. Our independent auditor for the year ended December 31, 2021 is Ernst & Young LLP (PCAOB ID: 42), located in Stamford, Connecticut, USA and our independent auditor for the year ended December 31, 2020 was BDO USA, LLP (PCAOB ID: 243), located in Stamford, CT, USA.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

The information required by this Item was previously provided in and is hereby incorporated under this Item by reference to the Company's Current Report on Form 8-K filed with the SEC on March 15, 2021.

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, 2021. 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, or 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 SEC's rules and forms. 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, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2021, 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, 2021, 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, 2021 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.

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 2022 (the "2022 Annual Meeting of Stockholders"), which we intend to file with the SEC within 120 days of the year ended December 31, 2021.

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 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2021.

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 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2021.

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 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2021.

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 2022 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the year ended December 31, 2021.

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	8/10/2021	
3.2	Amended and Restated Bylaws	8-K	001-38410	3.2	3/13/2018	
4.1	Description of the Registrant's Securities Registered Under Section 12 of the Exchange Act	10-K	001-38410	4.1	3/09/2020	
4.2	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-222990	4.2	2/26/2018	
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	3/09/2020	
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	3/12/2021	
10.3#	Amended and Restated Asset Contribution Agreement, effective November 7, 2017, by and between BioXcel Corporation and BioXcel Therapeutics, Inc.	S-1/A	333-222990	10.2	2/12/2018	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
10.4	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	8/23/2018	
10.5	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	
10.6†	2017 Equity Incentive Plan	S-1/A	333-222990	10.3	2/12/2018	
10.7†	Form of Incentive Stock Option Agreement under the 2017 Equity Incentive Plan	S-1/A	333-222990	10.4	2/12/2018	
10.8†	Form of Non-Statutory Stock option Agreement under the 2017 Equity Incentive Plan	S-1/A	333-222990	10.5	2/12/2018	
10.9†	BioXcel Therapeutics, Inc. 2020 Incentive Award Plan and forms of award agreements thereunder	10-Q	001-38410	10.1	8/14/2020	
10.10†	BioXcel Therapeutics, Inc. 2020 Employee Stock Purchase Plan	10-Q	001-38410	10.2	8/14/2020	
10.11†	Form of Indemnification Agreement with directors and executive officers	S-1/A	333-222990	10.6	2/12/2018	
10.12†	Employment Agreement, dated March 7, 2018 by and between BioXcel Therapeutics, Inc. and Vimal Mehta	8-K	001-38410	10.1	3/13/2018	
10.13†	Employment Agreement, dated February 12, 2018, by and between BioXcel Therapeutics, Inc. and Frank Yocca	S-1/A	333-222990	10.11	2/12/2018	
10.14†	Employment Agreement, effective October 2, 2017, by and between BioXcel Therapeutics, Inc. and Richard Steinhart	S-1/A	333-222990	10.12	2/12/2018	
10.15†	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	6/07/2018	
10.16†	Employment Agreement between William Kane and BioXcel Therapeutics, Inc., dated May 15, 2020.	10-Q	001-38410	10.3	8/14/2020	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
10.17†	Employment Agreement between Reina Benabou and BioXcel Therapeutics, Inc., dated June 21, 2020.	10-Q	001-38410	10.4	8/14/2020	
10.18†	Separation Agreement and General Release between Reina Benabou and BioXcel Therapeutics, Inc., dated July 28, 2021.	10-Q	001-38410	10.1	8/10/2021	
10.19†	Employment Agreement between Javier Rodriguez and BioXcel Therapeutics, Inc., dated February 15, 2021.	10-K	001-38410	10.19	3/12/2021	
10.20†	Employment Agreement between Matthew Wiley and BioXcel Therapeutics, Inc., dated January 12, 2022.					*
10.21†	Non-Employee Director Compensation Program	10-Q	001-38410	10.1	5/12/2020	
21.1	Subsidiaries of BioXcel Therapeutics, Inc.					*
23.1	Consent of Ernst & Young LLP					*
23.2	Consent of BDO USA, LLP; Stamford, CT; (PCAOB ID #243)					*
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.					*
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					*

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
	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.
* 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 10, 2022

By:
/s/ Vimal Mehta
Vimal Mehta
Chief Executive Officer
(Principal Executive Officer)

Dated: March 10, 2022

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, President, and Director *(Principal Executive Officer)*	March 10, 2022
/s/ RICHARD STEINHART Richard Steinhart	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 10, 2022
/s/ PETER MUELLER Peter Mueller, Ph.D.	Chairman of the Board of Directors	March 10, 2022
/s/ JUNE BRAY June Bray	Director	March 10, 2022
/s/ SANDEEP LAUMAS Sandeep Laumas, M.D.	Director	March 10, 2022
/s/ KRISHNAN NANDABALAN Krishnan Nandabalan, Ph.D.	Director	March 10, 2022
/s/ MICHAL VOTRUBA Michal Votruba	Director	March 10, 2022

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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 balance sheet of BioXcel Therapeutics, Inc. (the Company) as of December 31, 2021, the related statements of operations and stockholders' equity and cash flows for the year then ended, and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021, and the results of its operations and its cash flows for the year 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 audit. 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 audit 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 audit 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 audit 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 audit 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 audit provides a reasonable basis for our opinion.

/s/ Ernst & Young LLP

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

Stamford, Connecticut
March 10, 2022

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
BioXcel Therapeutics, Inc.
New Haven, CT

Opinion on the Financial Statements

We have audited the accompanying balance sheet of BioXcel Therapeutics, Inc. (the "Company") as of December 31, 2020, the related statements of operations, changes in stockholders' equity, and cash flows for the year ended December 31, 2020, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020, and the results of its operations and its cash flows for the year ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

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 audit 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 audit, 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 audit 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 audit 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 audit provides a reasonable basis for our opinion.

/s/ BDO USA, LLP

We served as the Company's auditor from 2017 to 2021.

Stamford, Connecticut

March 12, 2021

BIOXCEL THERAPEUTICS, INC.

BALANCE SHEETS

(amounts in thousands, except per share amounts)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets		
Cash and cash equivalents	$ 232,968	$ 213,119
Prepaid expenses	2,888	2,962
Other current assets	956	984
Total current assets	236,812	217,065
Property and equipment, net	1,294	1,273
Operating lease right-of-use assets	1,247	1,511
Other assets	86	87
Total assets	$ 239,439	$ 219,936
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 4,678	$ 3,979
Accrued expenses	11,492	7,469
Due to related party	204	157
Other current liabilities	293	237
Total current liabilities	16,667	11,842
Long-term portion of operating lease liabilities	1,105	1,398
Total liabilities	17,772	13,240
Commitments and contingencies (Note 11)		
Stockholders' equity		
Common stock, $0.001 par value, 100,000 and 50,000 shares authorized as of December 31, 2021 and December 31, 2020, respectively; 27,980 and 24,417 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	28	24
Preferred stock, $0.001 par value, 10,000 shares authorized; no shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	—	—
Additional paid-in-capital	467,427	345,529
Accumulated deficit	(245,788)	(138,857)
Total stockholders' equity	221,667	206,696
Total liabilities and stockholders' equity	$ 239,439	$ 219,936

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

BIOXCEL THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS

(amounts in thousands, except per share amounts)

	Year Ended December 31,	
	2021	**2020**
Operating expenses		
Research and development	52,708	57,995
General and administrative	54,227	24,302
Total operating expenses	106,935	82,297
Loss from operations	(106,935)	(82,297)
Other income (expense)		
Interest income	44	155
Interest expense	(40)	(27)
Net loss and comprehensive loss	$ (106,931)	$ (82,169)
Basic and diluted net loss per share attributable to common stockholders	$ (4.05)	$ (3.79)
Weighted average shares outstanding - basic and diluted	26,373	21,683

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

BIOXCEL THERAPEUTICS, INC.

STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

(amounts in thousands)

	Common Stock		Additional Paid in	Accumulated	
	Shares	Amount	Capital	Deficit	Total
Balance as of January 1, 2020	18,087	$ 18	$ 83,565	$ (56,688)	$ 26,895
Issuance of common shares, net of issuance costs of $17,815	6,300	6	255,779	—	255,785
Purchase and cancellation of shares from BioXcel LLC	(300)	—	(9,024)	—	(9,024)
Stock-based compensation	—	—	14,611	—	14,611
Exercise of stock options	330	—	598	—	598
Net loss	—	—	—	(82,169)	(82,169)
Balance as of December 31, 2020	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

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

BIOXCEL THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS

(amounts in thousands)

	Year ended December 31,	
	2021	**2020**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (106,931)	$ (82,169)
Reconciliation of net loss to net cash used in operating activities		
Depreciation and amortization	297	188
Loss on disposal of equipment	46	—
Stock-based compensation expense	19,455	14,611
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	103	(2,301)
Operating lease right of use assets	264	288
Accounts payable, accrued expenses, and other liabilities	4,850	3,197
Operating lease liabilities	(237)	(164)
Net cash used in operating activities	(82,153)	(66,350)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of equipment and leasehold improvements	(445)	(316)
Net cash used in investing activities	(445)	(316)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock, net of issuance costs	100,993	255,785
Purchase and cancellation of shares from BioXcel LLC	—	(9,024)
Exercise of stock options	1,454	598
Net cash provided by financing activities	102,447	247,359
Net increase in cash and cash equivalents	19,849	180,693
Cash and cash equivalents, beginning of the period	213,119	32,426
Cash and cash equivalents, end of the period	$ 232,968	$ 213,119
Supplemental cash flow information:		
Interest paid	40	27
Purchases of property and equipment in accounts payable and accrued expenses	22	104
Operating lease ROU assets obtained in exchange for operating lease liabilities	—	606

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

BIOXCEL THERAPEUTICS, INC.

NOTES TO FINANCIAL STATEMENTS

(in thousands, except per share amounts)

Note 1. Nature of the Business

BioXcel Therapeutics, Inc. ("BTI") is a clinical stage biopharmaceutical company focused on drug development that utilizes artificial intelligence to identify improved therapies in neuroscience and immuno-oncology. BTI's drug re-innovation approach leverages existing approved drugs and/or clinically validated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indices. BTI's two most advanced clinical development programs are BXCL501, a proprietary, orally dissolving, sublingual thin film formulation of the adrenergic receptor agonist dexmedetomidine ("Dex"), for the treatment of agitation and opioid withdrawal symptoms, and BXCL701, an orally administered, systemic innate immune activator for the treatment of aggressive forms of prostate cancer and advanced solid tumors that are refractory or treatment naïve to checkpoint inhibitors.

As used in these financial statements, unless otherwise specified or the context otherwise requires, the terms the "Company" or "BTI" refer to BioXcel Therapeutics, Inc., and "BioXcel, LLC " refer to BioXcel LLC and, its predecessor, BioXcel Corporation.

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

Certain reclassifications have been made to the prior year financial information to conform to the current period presentation. These reclassifications had no effect on the reported results of operations.

Impact of COVID-19 Pandemic

During the first quarter ended March 31, 2020, and continuing through December 31, 2021, the novel coronavirus disease, or COVID-19, was declared a pandemic and spread to multiple regions across the globe, including the United States and Europe. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen.

To date we have taken steps in line with guidance from the U.S. Centers for Disease Control and Prevention ("CDC") and the State of Connecticut to protect the health and safety of our employees and the community. In particular, we implemented a work-from-home policy for all employees and have restricted on-site activities to certain chemical, manufacturing and control ("CMC") and clinical trial activities. We continue to assess the impact of the COVID-19 pandemic to best mitigate risk and continue the operations of our business. Beginning late in the second quarter of 2020, we began to slowly bring our staff, in very limited numbers, back to our office. This modified return-to-work approach is continuing into 2022. We have taken steps to protect our workforce and have instituted strict work rules to protect our employees.

We continue to work closely with our clinical sites to monitor the potential impact of the evolving COVID-19 pandemic. We remain committed to our clinical programs and development plans. Other than Phase 2 clinical trial evaluating BXCL501 in patients with delirium through December 31, 2021, we have not experienced any significant delays to our ongoing or planned clinical trials, except for challenges in accessing elderly care facilities and ICU settings; however, this could rapidly change.

Note 2. Basis of Presentation

The Company's financial statements are prepared in accordance with Generally Accepted Accounting Principles in the United States of America ("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 Company's financial statements are prepared in accordance with GAAP. The preparation of the Company's financial statements requires it to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses in its financial statements and the accompanying notes. 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, 2021, and 2020, cash equivalents were comprised primarily of money market funds. Cash and cash equivalents held at financial institutions may at times exceed federally insured amounts. We believe we mitigate such risk by investing in or through major financial institutions.

Property and Equipment

Property and equipment are recorded at cost and depreciated and amortized 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 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 general and administrative expenses in net loss from operations in the statement of operations.

The Company follows the guidance provided by FASB ASC Topic 360-10, *Property, Plant, and Equipment*. 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. 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

We determine 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 our balance sheet.

ROU assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. As our lease did not provide an implicit rate, we used an incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. We use the implicit rate when readily determinable. The operating lease ROU asset also includes any prepaid lease payments made and excludes lease incentives. Our lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. Renewal options were not included in our calculation of the related asset and liability. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

Stock-Based Compensation

The Company accounts for stock-based compensation in accordance with ASC 718, "*Compensation—Stock Compensation,*" which requires the measurement and recognition of compensation expense based on estimated fair market values for all share-based awards made to employees and directors, including stock options. The Company's 2017 Equity Incentive Plan became effective in August 2017. The Company's 2020 Incentive Award Plan ("2020 Plan") became effective in May 2020. Following the effective date of the Company's 2020 Stock 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 option awards are valued at fair value on the date of grant and that fair value is recognized over the requisite service period using the accelerated attribution method. The estimated fair value of stock option awards was determined using the Black-Scholes option pricing model on the date of grant. Prior to the IPO, significant judgment and estimates were used to estimate the fair value of these awards prior to the IPO. Stock awards granted by the Company subsequent to the IPO are valued using market prices at the date of grant.

ASC 718 requires companies to estimate the fair value of share-based awards on the date of grant using an option-pricing model. The Black-Scholes option-pricing model was used as its method of determining fair value. This model is affected by the Company's stock price as well as assumptions regarding a number of subjective variables. These subjective variables include, but are not limited to, the expected stock price volatility over the term of the awards, and actual and projected employee stock option exercise behaviors. The value of the award is recognized as an expense in the statement of operations over the requisite service period using the accelerated attribution method. 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, facilities, supplies, external services, clinical study and manufacturing costs 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 as a result of the 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.

Expenses Accrued Under Contractual Arrangements

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. 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.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. 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 expenses, we estimate the time period over which services will be performed and the level of effort to be expended in each period, which is based on an established protocol specific to each clinical trial. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly. 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 expensed as incurred as general and administrative costs as recoverability of such expenditures is uncertain.

Fair Value of Financial Instruments

The Company applies the provisions of ASC 820, "*Fair Value Measurements and Disclosures*" for financial assets and liabilities measured on a recurring basis which requires disclosure that establishes a framework for measuring fair value. ASC 820 defines fair value 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. ASC 820 establishes 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). ASC 820 requires that fair value measurements be classified and disclosed in one of 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.

The carrying amounts of cash and accounts payable approximate fair value due to the short-term nature of these instruments.

As of December 31, 2021, and December 31, 2020, the Company had $232,968 and $213,119, respectively, in cash and U.S. government money market accounts (included in cash and cash equivalents) which was valued based on Level

1 inputs. There were no transfers between levels within the hierarchy during the year ended December 31, 2021 and December 31, 2020.

Earnings (Loss) per Share

Basic earnings (loss) per share ("EPS") is calculated in accordance with ASC 260, "*Earnings Per Share*," by dividing net income or loss attributable to common stockholders by the weighted average common stock outstanding. Diluted EPS is calculated by adjusting weighted average common shares outstanding for the dilutive effect of common stock options and warrants. In periods in which a net loss is recorded, no effect is given to potentially dilutive securities, since the effect would be antidilutive. Securities that could potentially dilute basic EPS in the future were not included in the computation of diluted EPS because to do so would have been 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, our chief operating decision maker has made such decisions and assessed performance at the company level as one segment.

Recent Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12*, Income Taxes (Topic 740)* 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 GAAP for other areas of accounting for income taxes by clarifying and amending existing guidance. ASU No. 2019-12 is effective for fiscal years beginning after December 15, 2020. The Company adopted ASU No. 2019-12 effective January 1, 2021. The adoption of ASU No. 2019-12 did not have a material impact on the Company's financial statements.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*. We adopted this standard effective January 1, 2020 on a prospective basis. ASU No. 2018-15 requires that certain implementation costs for cloud computing arrangements are capitalized and amortized over the term of associated hosted cloud computing arrangement service. ASU No. 2018-15 also provides classification guidance on these implementation costs as well as additional quantitative and qualitative disclosures. The adoption of ASU No. 2018-15 did not have an effect on the Company's 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: ASU No. 2018-19, ASU No. 2019-04 and No. ASU 2019-05 (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 for the Company, until fiscal year 2023. The Company does not expect that the adoption of ASU No. 2016-13 will have a material impact on its financial statements.

Note 4. 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, par value $0.001 per share (the "Common Stock"), having an aggregate offering price of up to $100,000 (the "Shares"), from time to time, through an "at the marketing 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 had received proceeds of $4,056, net of issuance costs of $500.

In July 2020, the Company sold in a registered offering 4,000 shares of its common stock at a public offering price of $50.00. The Company received proceeds of approximately $186,974, net of issuance costs of $13,026. Under the terms of the Underwriting Agreement entered into by the Company in connection with the July 2020 offering, certain stockholders of the Company granted the underwriters an option exercisable for thirty days to purchase up to an additional 600 shares of common stock at the public offering price less underwriting discounts and commissions, which was not exercised. The Company intends to use the net proceeds of the offering to fund ongoing clinical trials, commercialization preparation and for general corporate purposes.

In February 2020, the Company sold in a registered offering 2,300 shares of its common stock at a public offering price of $32.00 per share. The Company received proceeds of $68,811, net of issuance costs of $4,789. The Company used $9,024 of the proceeds to purchase and cancel 300 shares of common stock from BioXcel LLC.

Note 5. 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, or the Services Agreement, pursuit to which services provided by BioXcel LLC through its subsidiaries in India and the United States will continue indefinitely, as agreed upon by the parties. These services are primarily for drug discovery, chemical, manufacturing and controls cost, and administrative support.

Service charges recorded under this agreement for the year ended December 31, 2021 and 2020 were comprised as follows:

	Year Ended December 31,	
	2021	2020
Research and development	$ 1,184	$ 1,180
General and administrative	218	82
Total	$ 1,402	$ 1,262

As of December 31, 2021 and 2020, $204 and $157 related to these service charges is included in due to related parties in the Company's balance sheet, respectively.

Under the Services Agreement, the Company has an option, exercisable until March 12, 2023, 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. 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 milestones shall not exceed $10 million in the aggregate and not be payable prior to proof of concept in humans and (ii) commercialization milestones 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 through at least September 30, 2024. As of December 31, 2021, this option has not been exercised.

The Company paid $9,024 in February 2020 for the purchase and subsequent cancellation of 300 shares owned by BioXcel LLC.

Note 6. Earnings (Loss) Per Share

Basic earnings (loss) per share ("EPS") is calculated in accordance with ASC 260, "Earnings Per Share," by dividing net income or loss attributable to common stockholders by the weighted average common stock outstanding. Diluted EPS is calculated by adjusting weighted average common shares outstanding for the dilutive effect of common stock options. In periods in which a net loss is recorded, no effect is given to potentially dilutive securities, since the effect would be antidilutive. Securities that could potentially dilute basic EPS in the future were not included in the computation of diluted EPS because to do so would have been antidilutive. The calculations of basic and diluted net loss per share are as follows (in thousands, except per share amounts):

	Year Ended December 31,	
	2021	2020
Net loss (numerator)	$ (106,931)	$ (82,169)
Weighted average share, in thousands (denominator)	26,373	21,683
Basic and diluted net loss per share	$ (4.05)	$ (3.79)

Potentially dilutive securities outstanding consists solely of stock options. The Company had options outstanding to purchase 4,000 and 3,798 shares of common stock as of December 31, 2021 and 2020, respectively.

Note 7. Property and Equipment, net

A summary of property and equipment is as follows:

	December 31, 2021	December 31, 2020
Computers and related equipment	$ 167	$ 260
Furniture	572	369
Leasehold improvements	1,133	650
Work in process	24	356
	1,896	1,635
Accumulated depreciation	(602)	(362)
	$ 1,294	$ 1,273

Depreciation expense was $297 and $188 for the years ended December 31, 2021 and 2020, respectively.

Note 8. Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2021	December 31, 2020
Research and development expenses	$ 5,762	$ 3,264
Accrued compensation and benefits	3,968	2,066
Accrued professional expenses	1,324	1,288
Accrued taxes	302	697
Other accrued expenses	136	154
	$ 11,492	$ 7,469

Note 9. Stock-Based Compensation

2017 Equity Incentive Plan

The Company's 2017 Equity Incentive Plan (the "2017 Plan") became effective in August 2017. Following the effective date of the Company's 2020 Plan (as defined below), 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 Shareholders 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 authorized for issuance 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 as of immediately prior to the approval of the 2020 Plan by the Company's shareholders. Any shares of Common Stock which, as of 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. On January 1, 2021, the shares available for issuance under the 2020 Plan increased by 977 shares and on January 1, 2022, the shares available for issuance under the 2020 Plan increased by 1,119 additional shares pursuant to this provision.

Options granted under the 2020 Plan have a term of ten years with the vesting schedule determined by the Board of Directors, which is generally four years.

As of December 31, 2021, there were 648 shares available to be granted under the 2020 Plan.

A summary of the status of the Company's stock option activity for the year ended December 31, 2021 is presented below (in thousands, except per share amounts):

	Number of Shares	Weighted Average Exercise Price per Share
Outstanding as of January 1, 2021	3,798	$ 16.15
Granted	869	$ 37.26
Forfeited	(364)	$ 43.04
Cancelled	(19)	$ 55.38
Exercised	(284)	$ 5.12
Outstanding as of December 31, 2021	4,000	$ 18.89
Options vested and exercisable as of December 31, 2021	2,684	$ 9.58

As of December 31, 2021, the intrinsic value of options outstanding was $41,120. 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, 2021 and 2020 was $11,942 and $11,629, respectively. The total intrinsic value of stock options exercisable for the years ended December 31, 2021 and 2020 was $39,794 and $99,054, respectively.

The weighted average grant date fair value of options granted in 2021 and 2020 was $28.81 and $32.71, respectively.

The weighted average grant date fair value of options vested at December 31, 2021 was $7.05.

The weighted average remaining contractual life is 6.3 years for options exercisable. The weighted average remaining contractual life is 8.8 years for options outstanding.

Stock-Based Compensation

The fair value of options granted during the years ended December 31, 2021 and 2020 was estimated using the Black-Scholes option-pricing model with the following assumptions.

	For the Year Ended December 31, 2021	For the Year Ended December 31, 2020
Expected Term	5.50 years- 6.25 years	5.50 years- 6.25 years
Expected stock price volatility	95.00 % -98.00 %	79.02 % -86.71 %
Risk-free rate of interest	0.96 % - 1.37 %	0.33 % - 2.34 %
Expected dividend	0.0 % - 0.0 %	0.0 % - 0.0 %

Prior to the Company's IPO, it did not have a history of market prices of its common stock and, as such, volatility is estimated using historical volatilities of similar public companies. In 2021, the Company began using a combination of the historical volatility of similar public companies and the limited historical information related to the Company's common stock. The expected term of the employee 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 0% 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 based on the United States 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 under the 2017 Plan and the 2020 Plan of $19,455 and $14,611 for the years ended December 31, 2021 and 2020, respectively.

Unrecognized compensation expense related to unvested awards as of December 31, 2021 was $18,738 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 1.7 years.

Total stock-based compensation charges were approximately $19,455 and $14,611 for the years ended December 31, 2021 and 2020, respectively. The Company charged $6,657 and $12,798 to research and development and general and administrative expense for the year ended December 31, 2021, respectively. The Company charged $6,020 and $8,591 to research and development and general and administrative expense for the year ended December 31, 2020, respectively.

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 Shareholders 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. 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 market value of a share on the first trading day or on the last trading day of the applicable offering period, whichever is lower. On January 1, 2021, the shares available for issuance under the 2020 ESPP increased by 244 shares and 344 shares were available at December 31, 2021 and on January 1, 2022, the shares available for issuance under the ESPP increased by 156 additional shares pursuant to this provision. To date, no shares have been sold under the ESPP.

Note 10. Leases

In August 2018, the Company entered into an agreement to lease approximately 11,040 square feet of space on the 12th floor of the building located at 555 Long Wharf Drive, New Haven, Connecticut (the "12th Floor Lease) which was effective February 22, 2019. The 12th Floor Lease expires in February 2026. Payments under the Company's lease agreement are fixed.

In August 2020, the Company entered into an amendment to the 12th Floor Lease wherein the Company leased an additional 7,245 square feet of space on the 12th floor of the building located at 555 Long Wharf Drive, New Haven, Connecticut (the "12th Floor Lease Amendment"). The 12th Floor Lease Amendment expires in February 2026. Payments under the Company's lease amendment agreement are fixed.

The future minimum annual lease payments under these operating leases as of December 31, 2021 are as follows:

Year ending December 31,	Amount
2022	363
2023	372
2024	381
2025	391
2026	65
Thereafter	-
Total lease payments	1,572
Less imputed interest	(174)
Total lease liability	1,398
Less current portion of lease liability	(293)
Long-term portion operating lease liability	$ 1,105

The current portion of the Company's operating lease liability of $293 as of December 31, 2021 is included in other current liabilities on the balance sheet.

The Company recorded lease expense related to its operating lease right-of-use asset of $365 and $345 for the years ended December 31, 2021 and 2020, respectively.

The Company has an option to renew the lease for one additional five-year term at 95% of the then-prevailing market rates but not less than the rental rate at the end of the initial lease term. The renewal option is not included in the right-of-use asset.

Note 11. 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, 2021, there were no matters which would have a material impact on the Company's financial results.

The Company received a demand letter pursuant to Section 220 of the Delaware General Corporation Law ("DGCL") from a stockholder seeking disclosure of certain of the Company's records. The Company responded to those demands, stating its belief that the demand letter failed to fully comply with the requirements of Section 220 of the DGCL. On June 15, 2021, the stockholder filed a complaint in Delaware Chancery Court seeking to compel inspection of books and records pursuant to Section 220 of the DGCL. Pursuant to a negotiated settlement agreement, the matter was dismissed with prejudice on August 10, 2021.

Note 12. 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.

The significant components of the Company's net deferred tax assets at December 31, 2021 and 2020 are shown below. 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.

	2021	2020
Deferred tax assets:		
Federal net operating losses	$ 29,157	$ 8,547
State net operating losses	8,213	2,411
Stock options	7,461	3,998
Tax credits	7,102	4,895
Capitalized R&D	18,880	21,249
Accrued expense	1,026	599
Depreciation	17	(11)
Lease Accounting - liability	376	440
Unrealized gain	3	—
Valuation allowance	(71,899)	(41,721)
Total deferred tax assets	336	407
Deferred tax liabilities:		
Right-of-use assets	(336)	(407)
Total deferred tax liabilities	(336)	(407)
Net deferred tax asset (liability)	$ —	$ —

The income tax benefit for the year ended December 31, 2021 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 Company's valuation allowance.

A reconciliation between the Company's effective tax rate and the federal statutory rate for the years ended December 31, 2021 and 2020 are as follows:

	2021	2020
Federal statutory rate	21.0 %	21.0 %
Stock based compensation	0.1 %	0.9 %
Federal and state credits	2.1 %	3.7 %
State taxes	5.8 %	6.8 %
Other	(0.7)%	(0.2)%
Valuation allowance	(28.3)%	(32.2)%
	— %	— %

At December 31, 2021, the Company had approximately $138,843 of gross federal and $138,614 of gross state net operating loss carry-forwards. If not utilized, the federal and state net operating loss carry-forwards will begin to expire in 2037. The federal net operating loss of $136,197 incurred after December 31, 2017 will be carried forward indefinitely. The utilization of such net operating loss carry-forwards and realization of tax benefits in future years depends predominantly upon having taxable income. The Company also has approximately $6,445 of federal research and development credits which will begin to expire in 2037 if not utilized.

Utilization of the net operating loss, or NOL, and research tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that has occurred or that could occur in the future, as required by Section 382 of the Code, as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and research tax 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 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 of a company by certain stockholders or public groups. To date, the company's NOL's have not been subject to the Section 382 limitation.

Entities are also required to evaluate, measure, recognize and disclose any uncertain income tax provisions taken on their income tax returns. The Company has analyzed its tax positions and has concluded that as of December 31, 2021, there were no uncertain positions. The Company's U.S. federal and state net operating losses 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 net operating losses from prior years opens the relevant year to audit by the IRS and/or state taxing authorities. The Company did not have any unrecognized tax benefits and has not accrued any interest or penalties for the 12 months ended December 31, 2021 and 2020.

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, 2021 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 10, 2022

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, 2021 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 10, 2022

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, 2021, 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 10, 2022

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, 2021, 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 10, 2022

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

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EXECUTIVE OFFICERS

Vimal D. Mehta, Ph.D.
President and Chief Executive Officer

Richard I. Steinhart
Senior Vince President and Chief Financial Officer

Matt Wiley
Senior Vice President and Chief Commercial Officer

Frank D. Yocca, Ph.D.
Senior Vice President and Chief Scientific Officer

Vincent J. O'Neill, M.D.
Senior Vice President and Chief Medical Officer

Javier Rodriguez
Senior Vice President, Chief Legal Officer, and Corporate Secretary

BOARD OF DIRECTORS

Peter Mueller, Ph.D.
Chairman of the Board of Directors of BioXcel Therapeutics, Inc., President of the Mueller Health Foundation

June Bray
Former Senior Vice President, Global Regulatory Affairs and Medical Writing at Allergan

Vimal D. Mehta, Ph.D.
President and Chief Executive Officer of BioXcel Therapeutics, Inc.

Krishnan Nandabalan, Ph.D.
President, Secretary and Chief Scientific Officer of BioXcel LLC

Sandeep Laumas, M.D.
Chief Financial Officer and Chief Business Officer of Instil Bio, Inc.

Michal Votruba, M.D.
Director of Gradus, RSJ Life Sciences Fund

AVAILABLE INFORMATION

We make our filings with the Securities and Exchange Commission (SEC) and other information about the Company available free of charge under the Investor Relations section of our website, www.bioxceltherapeutics.com. Our filings with the SEC may also be accessed free of charge on the SEC's public website, www.sec.gov.

STOCK TRANSFER AGENT

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