UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

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

Commission File Number: 001-39655

GALECTO, INC.

(Exact name of Registrant as specified in its Charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**37-1957007** **(I.R.S. Employer Identification No.)**
Ole Maaloes Vej 3 **DK-2200 Copenhagen N** **Denmark**	**N/A**
75 State Street, Suite 100 **Boston, Massachusetts** **(Address of principal executive offices)**	**02109** **(Zip Code)**

Registrant's telephone number, including area code: (+45) 70 70 52 10

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	GLTO	The Nasdaq Global Select Market

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

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Market on June 30, 2022, was $37.5 million.

The number of shares of Registrant's Common Stock outstanding as of March 6, 2023 was 25,673,474.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2023 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2022. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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Summary of Material Risks Associated with Our Business

Our business is subject to numerous material and other risks and uncertainties that you should be aware of in evaluating our business. These risks include, but are not limited to, the following:

- We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future.
- We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs, future commercialization efforts or other operations.
- Our business is highly dependent on the success of our product candidates GB0139, GB1211 and GB2064, as well as any other product candidates that we advance into the clinic. All of our product candidates may require significant additional preclinical and clinical development before we may be able to seek regulatory approval for and launch a product commercially.
- If we continue to encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- Our ongoing and future clinical trials may reveal significant adverse events or unexpected drug-drug interactions not seen in our preclinical studies and may result in a safety profile that could delay or prevent regulatory approval or market acceptance of any of our product candidates.
- The design or execution of our ongoing and future clinical trials may not support marketing approval or commercialization.
- We may not be successful in our efforts to identify or discover additional product candidates in the future.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- Even if we obtain U.S. Food and Drug Administration, or FDA, approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, or U.S., which would limit our ability to realize their full market potential.
- Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.
- We rely and expect to continue to rely on third parties to conduct certain aspects of our ongoing and future preclinical studies and clinical trials, including investigator-sponsored clinical trials of our product candidates. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.
- The price of our stock may be volatile, and you could lose all or part of your investment.
- If our common stock is delisted from The Nasdaq Global Select Market, the liquidity of our common stock would be adversely affected and the market price of our common stock could decrease.
- If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

The material and other risks summarized above should be read together with the text of the full risk factors below and in the other information set forth in this Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the Securities and Exchange Commission. If any such material and other risks and uncertainties actually occur, our business, prospects, financial condition and results of operations could be materially and

adversely affected. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, prospects, financial condition and results of operations.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including "Business" in Item 1, "Risk Factors" in Item 1A and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Item 7 includes "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "may," "could," "will," "would," "should," "expect," "plan," "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "project," "continue," "potential," "ongoing," "goal," or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements regarding:

- the success, cost and timing of our product development activities and planned initiation and completion of clinical trials of our most advanced product candidate, GB0139, and our other current fibrosis and oncology product candidates, including GB2064 and GB1211, and any future product candidates;
- our need to raise additional funding;
- our ability to obtain regulatory approval for our current or future product candidates that we may identify or develop;
- our ability to ensure adequate supply of our current or future product candidates;
- our ability to maintain third-party relationships necessary to conduct our business;
- our heavy dependence upon the success of our research to generate and advance additional product candidates;
- our ability to establish an adequate safety or efficacy profile for our current or future product candidates that we may pursue;
- the implementation of our strategic plans for our business, our current or future product candidates we may develop and our technology;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- the rate and degree of market acceptance and clinical utility for our current or future product candidates we may develop;
- our estimates about the size of our market opportunity;
- our estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to maintain and establish collaborations;
- our financial performance and liquidity;
- our ability to effectively manage our potential growth;
- developments relating to our competitors and our industry, including the impact of government regulation;
- our ability to retain the continued service of our key professionals and consultants and to identify, hire and retain additional qualified professionals;
- our ability to maintain adequate internal controls over financial reporting;

- the effects of global economic uncertainty and financial market volatility caused by economic effects of rising inflation and interest rates, the COVID-19 pandemic, geopolitical instability, changes in international trade relationships and conflicts, such as the ongoing conflict between Russia and Ukraine, on any of the foregoing or other aspects of our business or operations; and

- other risks and uncertainties, including those listed under the section titled "Risk Factors."

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other 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 these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part II, Item 1A - "Risk Factors" below and for the reasons described elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties, and assumptions relating to our operations, results of operations, industry, and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. 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 drugs, including data regarding the estimated size of those markets, their projected growth rates, and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections, 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 these industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by third parties, industry, medical and general publications, government data, and similar sources. In some cases, we do not expressly refer to the sources from which these data are derived.

Except where the context otherwise requires, in this Annual Report on Form 10-K, "we," "us," "our," "Galecto," and the "Company" refer to Galecto, Inc. and, where appropriate, its consolidated subsidiaries.

Trademarks

We have applied for various trademarks that we use in connection with the operation of our business. This Annual Report on Form 10-K includes trademarks, service marks, and trade names owned by us or other companies. All trademarks, service marks, and trade names included in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, the trademarks and trade names in this report may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company developing novel small molecule therapeutics that are designed to target the biological processes that lie at the heart of cancer and fibrotic diseases. Our strategy is to focus on diseases without disease-modifying treatment options and where there is a high unmet medical need. We are concentrating on the development of a new class of medicines: small molecule inhibitors of galectin-3 and lysyl oxidase-like 2, or LOXL2, that target underlying biology for the treatment of multi-factorial diseases like cancer and fibrotic diseases. Galectin proteins, and especially galectin-3, are highly expressed in many cancers, where they promote cancer progression, and fibrotic diseases, where they reduce organ function. The collagen cross-linking enzyme LOXL2 builds the backbone of fibrotic tissue by cross-linking collagen and elastin molecules and has been linked to cancer growth, metastasis and fibrosis. Our product candidates are designed to modulate multiple disease pathways simultaneously by inhibiting the master drivers of the cancer and fibrotic cascades. We believe our galectin and LOXL2 product candidates are distinct from the current generation of anti-cancer and anti-fibrotic agents and have the potential to significantly improve patient outcomes for these complex diseases.

During the second half of 2022, we reported Phase 2 trial data for two of our product candidates. In September 2022, we announced data from a planned intermediate assessment from our Phase 2a trial of GB2064 for myelofibrosis, which we refer to as the MYLOX-1 trial, where four out of five evaluable myelofibrosis patients who received GB2064 monotherapy experienced a ≥ 1-grade reduction in collagen fibrosis of the bone marrow. We believe that this level of reduction in collagen fibrosis has not been shown in any other clinical trial and is an improvement suggesting that GB2064 could impact the progression of the disease and be disease-modifying. In the fourth quarter of 2022, we announced topline results from our Phase 1b/2a trial of GB1211 in patients with decompensated liver cirrhosis, which we refer to as the GULLIVER-2 trial, that showed statistically significant reductions in liver enzymes after 12 weeks of treatment and statistically significant reductions in biomarkers of inflammation and apoptosis, which are processes that are believed to be central to severe liver disease. We believe that this is the first study in a population of Child-Pugh Class B decompensated cirrhosis patients of non-viral etiology to show changes in a series of liver parameters that are potentially clinically meaningful. We currently have three ongoing Phase 2 clinical trials for GB0139, GB2064 and GB1211.

Our most advanced product candidate, GB0139, is an inhaled small molecule inhibitor of galectin-3, one of the key regulators of fibrosis that controls the pro-fibrotic activity of TGF-β. Overexpression of galectin-3 is ubiquitous in fibrotic tissue, including in fibrotic lung tissue, and is linked to both disease severity and disease progression, as well as acute exacerbations of idiopathic pulmonary fibrosis, or IPF. We are initially developing GB0139 for the treatment of IPF, a life-threatening progressive fibrotic disease of the lung. IPF affects approximately 100,000 people in the United States, but limited treatment options have been associated with significant side effects, leading to poor therapeutic adherence or dose reduction. In our clinical trials completed to date, we found orally-inhaled GB0139 to be generally well-tolerated and it inhibited galectin-3 in the lungs in a dose-dependent manner. We also observed that GB0139 decreased systemic levels of a range of plasma biomarkers, such as YKL-40 and platelet-derived growth factor, or PDGF, that have been linked to mortality, disease severity and/or progression in IPF. We are currently conducting a 52-week randomized, double-blind, multicenter, parallel, placebo-controlled Phase 2b trial investigating the safety and efficacy of GB0139 in patients with IPF, which we refer to as the GALACTIC-1 trial. We completed enrollment during the second quarter of 2022 and expect topline results to be available in mid-2023.

GB2064 is a selective oral small molecule inhibitor of LOXL2 that we are initially developing for the treatment of myelofibrosis, a malignant disease of the bone marrow in which progressive fibrosis reduces the ability to form blood cells in the bone marrow. Myelofibrosis is one of several types of cancer and multiple fibrotic diseases in which expression of LOXL2 is significantly increased. Unlike current treatment options for myelofibrosis, we believe that GB2064 has the potential to be a disease-modifying therapy as it is designed to have a direct impact on the fibrotic process and slow the progression of the disease. We are currently conducting a Phase 2a MYLOX-1 trial examining GB2064 in myelofibrosis and, in the third quarter of 2022, we announced results from a planned intermediate assessment of the first five patients who had completed at least six months of treatment with GB2064. Four of the five patients experienced a ≥ 1-grade reduction in collagen fibrosis of the bone marrow, an improvement suggesting that GB2064 could impact the progression of the disease and potentially be disease modifying. All four patients who experienced a ≥ 1-grade reduction in collagen fibrosis also showed stable hematological parameters (hemoglobin, white blood cell count, and thrombocytes) and stable spleen volume over the six month treatment period, and none required

transfusion. We expect topline results from the MYLOX-1 trial to be available by the end of 2023 and are beginning to plan for the next steps in clinical development, which we expect could include combining GB2064 with another myelofibrosis treatment.

GB1211 is a selective oral small molecule inhibitor of galectin-3 and is chemically distinct from GB0139. We believe GB1211 has the potential to treat multiple types of fibrosis and oncology indications. Within the field of fibrotic diseases, our initial target indication for GB1211 is liver cirrhosis, a severe, progressive disease that ultimately leads to liver failure and for which there are limited treatment options and no FDA-approved disease modifying therapeutics available. In the fourth quarter of 2022, we announced topline results from the Phase 1b/2a GULLIVER-2 trial of GB1211 in severe liver cirrhosis classified as Child-Pugh B, which is also referred to as decompensated liver cirrhosis. Topline results showed statistically significant reductions in ALT ($p<0.0005$), AST ($p<0.005$) and GGT ($p<0.05$), with encouraging reductions for ALP ($p<0.09$), after 12 weeks of treatment, and included reductions in galectin-3 ($p<0.05$) and CK-18 (M65) ($p<0.002$), which are markers of inflammation and of apoptosis. These processes are believed to be central to the ongoing disease progression in liver cirrhosis. Bilirubin, albumin, international normalized ratio (INR) and other biochemical measurements remained stable. ALT reductions were observed after seven days of treatment and the liver enzyme levels continued to decrease over the 12 weeks of treatment. These liver enzyme levels remained decreased compared to baseline two weeks after the study's conclusion, suggesting durable effects and a decrease in liver inflammation. GB1211 generally exhibited a favorable tolerability profile. The consistency of the changes and the progressive improvement observed in this trial lead us to believe that a broader study in patients with compensated and/or decompensated cirrhosis could show wider effects, providing a potential regulatory path as the first FDA-approved therapy for liver cirrhosis.

GB1211 is also being studied in oncology, where inhibition of galectin-3 has the potential to both directly reduce tumor growth as well as increase the immune mediated eradication of tumors, and is believed to increase T-cell recruitment and activation in the tumor microenvironment. We believe that high galectin-3 expression may be one of the important reasons why many patients experience checkpoint inhibitor resistance, and that the inhibition of galectin-3 could lead to an increase in the efficacy of checkpoint inhibitors in cancer patients with high galectin-3 expression. We presented preclinical data at the 2022 American Society of Clinical Oncology Annual Meeting that showed that GB1211 reversed a galectin-3 induced blockage of the checkpoint inhibitors atezolizumab and pembrolizumab, and exhibited synergistic effects with these checkpoint inhibitors. Our initial target indication for GB1211 in oncology is non-small cell lung cancer, or NSCLC, a cancer indication with high unmet medical need. In the fourth quarter of 2021, we announced that we had entered into a clinical trial supply agreement with F. Hoffmann-La Roche Ltd, or Roche, for our Phase 2a trial of GB1211 in combination with atezolizumab, marketed by Roche as Tecentriq®, a programmed death-ligand 1 (PD-L1) checkpoint inhibitor for the first-line treatment of NSCLC, which we refer to as the GALLANT-1 trial. We initiated Part A of this trial, an open-label study to select the dose of GB1211 to be used with atezolizumab, in the second quarter of 2022. We expect to release interim safety data from this part of the GALLANT-1 trial in the second quarter of 2023. Part B of this trial is designed to evaluate the safety and tumor shrinkage (based on RECIST criteria) of the combination of the selected dose of GB1211 and atezolizumab and we expect topline results to be available in the first half of 2024.

In October 2022, we expanded our focus on additional oncology indications and entered into an agreement with Providence Portland Medical Center's Earle A. Chiles Research Institute (EACRI) to evaluate the safety and efficacy of GB1211 in combination with pembrolizumab, marketed by Merck as Keytruda®. This planned, randomized, double-blind placebo controlled, investigator-initiated Phase 2 trial is expected to evaluate whether the addition of GB1211 increases the response rate of pembrolizumab in metastatic melanoma and head and neck squamous cell carcinoma (HNSCC) patients. This trial is expected to begin in the second half of 2023 and topline results could be reported as early as 2025.

Our Clinical Stage Drug Development Pipeline

We own global development and commercialization rights to all of the product candidates in our pipeline. The chart below summarizes key information about our programs.

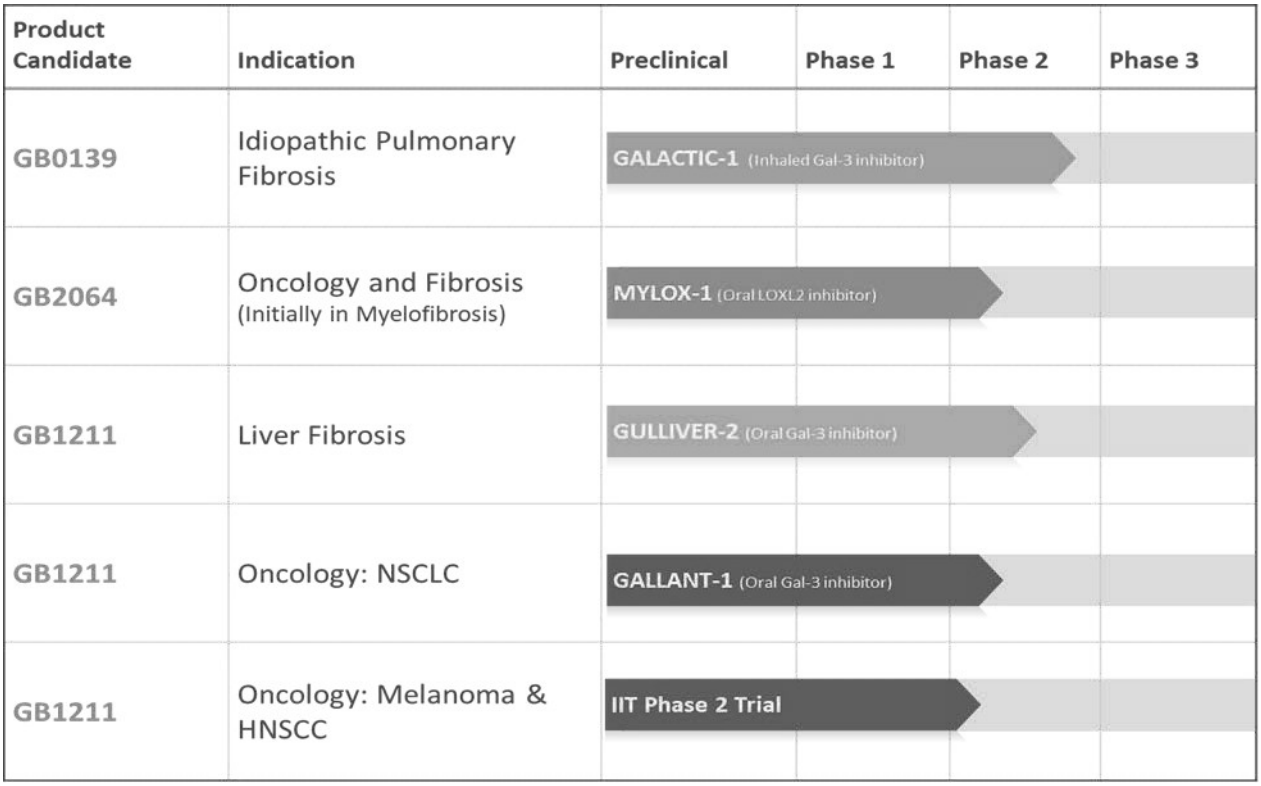


Figure 1. Galecto Clinical Pipeline

We are also progressing several preclinical assets targeting galectin-3 and other galectin proteins that have been associated with disease.

GB0139 (Idiopathic Pulmonary Fibrosis, IPF) – GALACTIC-1 Trial

Our most advanced product candidate, GB0139, is an inhaled small molecule inhibitor of galectin-3 that is designed to be administered via a generic dry powder inhaler. GB0139 is designed to target galectin-3, one of the key regulators of fibrosis that controls the pro-fibrotic activity of TGF-β. The overexpression of galectin-3 is ubiquitous in fibrotic tissue, including in fibrotic lung tissue, and is linked to both disease severity and disease progression, as well as acute exacerbations of IPF. We are currently developing GB0139 for the treatment of IPF, a life-threatening progressive fibrotic disease of the lung, but we plan to further develop GB0139 with the goal of treating other severe lung diseases driven by galectin-3. While there are currently two approved therapies for the treatment of lung fibrosis, they have been shown to only have a modest impact on slowing the progression of the disease and have not conclusively shown an impact on survival. Both therapies have been associated with significant tolerability type of side effects leading to poor therapeutic adherence and dose reductions. There are no therapeutics approved that specifically target galectin-3. GB0139 for the treatment of IPF has been granted Orphan Drug Designation by both U.S. and European regulatory authorities.

In our clinical, preclinical and *in vitro* testing to date, we have demonstrated that GB0139 can directly target galectin-3 in the lungs and markedly lowers the systemic plasma levels of biomarkers of fibrosis in IPF patients. In our Phase 1/2a trial in both healthy volunteers and IPF patients, GB0139 was generally well-tolerated, showed consistent and tight pharmacokinetics measured as plasma levels of the compound, and showed target engagement with the inhibition of galectin-3 in the lungs of IPF patients in a dose-dependent manner. Our clinical trials completed to date have found that orally inhaled GB0139 also decreased systemic levels of a range of plasma biomarkers, such as the glycoprotein YKL-40 and PDGF, that have been linked to mortality, disease severity and/or progression in IPF.

Galectin-3 overexpression has been associated with increased severity and poor prognosis in a number of viral infections, including COVID-19. In addition, viral infections are associated with the onset of acute exacerbations of IPF. in 2021, GB0139 was investigated in a Phase 2a trial as part of the University of Edinburgh's rapid experimental program for COVID-19 respiratory failure, which we refer to as the DEFINE trial. The trial met its primary endpoint with results showing that inhaled GB0139 had an acceptable tolerability profile when used in combination with standard of care (dexamethasone, remdesivir and anticoagulant therapy) in hospitalized patients with COVID-19 pneumonia requiring oxygen therapy. Despite being breathless and requiring oxygen, patients receiving GB0139 plus standard of care were able to inhale and achieve consistent exposure of GB0139 and required significantly less oxygen when compared to patients receiving standard of care alone. The 10mg dose of GB0139, dosed twice a day for 2 days and subsequently once a day for up to 14 days, which was higher than the current 3mg dose being used in the GALACTIC-1 trial, was generally well-tolerated and no treatment-related serious adverse events were reported. Furthermore, inhaled GB0139 led to a significant reduction of galectin-3 levels in patients with COVID-19 compared to standard of care, demonstrating target engagement, and showed reduced plasma levels of other key biomarkers associated with severe disease and a poor prognosis, including key cytokines CXCL10, IL-6, IL-10 and TNFα and markers of fibrosis, YKL-40 and PAI-1. The study showed that galectin-3 inhibition may be a way to reduce virally induced systemic inflammation and other hallmarks of severe viral disease.

We are currently conducting the GALACTIC-1 trial, a 52-week randomized, double-blind, multicenter, parallel, placebo-controlled Phase 2b trial investigating the safety and efficacy of GB0139 in patients with IPF. The primary endpoint of the trial is to assess the annual rate of decline in forced vital capacity, or FVC, over 52 weeks, which is the regulatory endpoint identified for IPF therapy approval. Reduction in the decline of FVC is the endpoint that was accepted by the FDA for the approval of both nintedanib, marketed as Ofev® by Boehringer Ingelheim, and pirfenidone, marketed as Esbriet® by Roche/Genentech, which are the only current therapeutic treatments for IPF. In March 2021, we were notified by the trial's data safety monitoring board, or the DSMB, who had access to unblinded safety and efficacy data, to discontinue dosing of GB0139 in patients who were also receiving nintedanib or pirfenidone, and in patients receiving the monotherapy GB0139 10mg dose. The DSMB's determination was based on an identification of an imbalance in the serious adverse events across the study groups, but not an imbalance between the groups in mortality. During the second quarter of 2021, we amended the study protocol to reflect these changes, and in July 2021 we resumed recruitment of patients for the GALACTIC-1 trial. The study has completed enrollment of the 144 patients provided for in the amended study protocol, and all of these patients have received or are receiving either the 3mg dose of GB0139 or placebo. We expect topline results to be available in mid-2023.

GB2064 (Myelofibrosis) – MYLOX-1 Trial

We are developing GB2064, a selective oral small molecule inhibitor of LOXL2. In contrast to previous attempts to inhibit LOXL2 with a monoclonal antibody, such as simtuzumab, GB2064 is designed to inhibit the enzymatic center of the LOXL2 molecule to a much higher degree and shut down collagen cross-linking more effectively. Our initial focus is developing GB2064 for the treatment of myelofibrosis, a malignant disease of the bone marrow in which progressive fibrosis reduces the ability to form blood cells in the bone marrow. This indication allows us to take and examine serial bone marrow biopsies where we can study GB2064's potential impact on bone marrow collagen. Myelofibrosis is one of several types of cancer and multiple fibrotic diseases in which expression of LOXL2 is significantly increased. Myelofibrosis is a disease with significant morbidity and mortality that affects between 16,000 and 18,500 patients in the United States. The current standard of care for myelofibrosis consists of inhibitors of the JAK2 protein kinase, which alleviate the disease symptoms through inhibition of cell proliferation but do not directly target or reduce the fibrosis of the bone marrow. As a result, a significant unmet need remains. We believe that GB2064 has the potential to be a disease-modifying therapy, as it is designed to have a direct impact on the fibrotic process and slow the progression of the disease, as opposed merely to treating symptoms, such as splenomegaly.

In preclinical studies, GB2064 showed activity in multiple models of fibrosis including lung, liver and kidney fibrosis. GB2064 has successfully completed a Phase 1 trial in 78 healthy volunteers, in which orally-administered GB2064 led to dose-dependent inhibition of LOXL2 in serum.

During the third quarter of 2021, we initiated the Phase 2a MYLOX-1 trial examining GB2064 for the treatment of myelofibrosis. The primary endpoint of this trial is safety and secondary endpoints include measurements of drug levels in the bone marrow and grade of fibrosis, improvement of anemia and/or thrombocytopenia and assessment of spleen and liver size. During the third quarter of 2022, we announced data from a planned intermediate assessment. As part of this assessment, we evaluated results from the first five patients who had completed at least six months of treatment with GB2064 and who had repeated valid bone marrow biopsies. In the intermediate assessment, four out of five evaluable myelofibrosis patients who received GB2064 monotherapy for at least six months experienced a ≥ 1-grade reduction in collagen fibrosis of the bone marrow, an improvement suggesting that GB2064 could impact the progression of the disease and potentially be disease modifying. We believe that this ≥ 1-grade reduction in collagen fibrosis has not been shown in any other clinical trial, signaling both an opportunity in myelofibrosis and, more generally, a wider opportunity for LOXL2 inhibition in other cancers and fibrotic diseases. All four patients who experienced a ≥ 1-grade reduction in fibrosis score also showed stable hematological parameters

(hemoglobin, white blood cell count, and thrombocytes) and stable spleen volume over the six month treatment period, and none required transfusion. As of the date of the planned intermediate assessment, sixteen patients in the MYLOX-1 trial had been dosed with GB2064, of which eight patients had completed or continued to receive treatment and eight patients had either discontinued treatment as a result of an adverse event or disease progression. The most commonly observed treatment-related adverse events were gastrointestinal in nature and were manageable in most patients with standard therapy. In the five patients who completed at least six months of treatment with GB2064 and valid bone marrow biopsies, there were no treatment-related serious adverse events, while in the entire trial population, the only possibly treatment-related serious adverse event was a case of fall.

The data from the intermediate assessment of the MYLOX-1 trial suggest that the LOXL2 mechanism may be a way to reduce fibrosis, which we believe has not been shown with any FDA-approved therapy. We continue to enroll patients in the MYLOX-1 trial and expect topline results from the MYLOX-1 trial to be available by the end of 2023. Because the MYLOX-1 trial has already exceeded the pre-defined target of a $\geq$ 1 grade reduction in collagen fibrosis in at least three patients, we may determine to enroll fewer patients than the sixteen evaluable patients provided for in the protocol. Given that we have already shown bone marrow collagen reduction and a manageable clinical tolerability profile, we are beginning to plan for next steps in clinical development, which we expect could include combining GB2064 with another myelofibrosis treatment.

The data from the intermediate assessment of the MYLOX-1 trial and the published literature on the LOXL2 mechanism suggest that LOXL2 inhibition may also be important in other solid and liquid tumor types as well as in fibrotic diseases.

GB1211 (Liver Cirrhosis and Oncology Indications) – GULLIVER-2 and GALLANT-1 Trials

GB1211 is a selective oral small molecule inhibitor of galectin-3 and is chemically distinct from GB0139. We believe GB1211 has the potential to treat multiple types of fibrosis and oncology indications. GB1211 demonstrated antifibrotic activity and an anticancer effect in multiple preclinical models and was evaluated in a Phase 1 trial in 78 healthy volunteers. In the Phase 1 trial, GB1211 was well-tolerated and showed dose-dependent pharmacokinetics.

Liver Cirrhosis

Our initial target indication for GB1211 in fibrosis is liver cirrhosis, a severe, progressive disease that ultimately leads to liver failure and for which there are limited treatment options. While the historical view was that established fibrosis is very difficult to impact, our preclinical data suggest that galectin-3 inhibition could reduce established fibrosis and the disease processes that drive the disease progression.

During the fourth quarter of 2022, at the American Association for the Study of Liver Diseases' (AASLD) The Liver Meeting® 2022, we announced topline results from our Phase 1b/2a GULLIVER-2 trial of GB1211 that is focused on safety and effect on liver function and fibrosis biomarkers in patients with decompensated liver cirrhosis. These topline results showed statistically significant reductions in ALT ($p<0.0005$), AST ($p<0.005$) and GGT ($p<0.05$), with encouraging reductions for ALP ($p<0.09$), after 12 weeks of treatment. Patients treated with GB1211 also demonstrated improvement and consistent signs of activity across biochemical liver function markers and markers of target engagement, apoptosis, and fibrosis, including reductions in galectin-3 ($p<0.05$) and CK-18 (M65) ($p<0.002$). Bilirubin, albumin, international normalized ratio (INR) and other biochemical measurements remained stable. These findings suggest that GB1211 provided liver cell protection and improved liver status, further supporting clinical development in severe liver disease. Liver enzyme (ALT, AST and GGT) reductions were observed after seven days of treatment and continued to decrease over the 12 weeks of treatment. These liver enzyme levels remained decreased compared to baseline two weeks after the study's conclusion, suggesting durable effects and a decrease in liver inflammation.

GB1211 exhibited a favorable tolerability profile in patients with decompensated liver cirrhosis in the GULLIVER-2 trial. Five of 15 patients on GB1211 and four of 15 patients on placebo reported nine and eight treatment-emergent adverse events (TEAEs), respectively. Three serious TEAEs consistent with severe liver disease were observed in one patient (2 after cessation of active therapy) on GB1211 and were deemed to be unrelated to GB1211.

The consistency of the reductions in liver enzymes shown in this severe form of liver cirrhosis, the progressive improvement we observed over 12 weeks and the favorable safety profile observed in the GULLIVER-2 trial lead us to believe that a broader study in patients with compensated and/or decompensated cirrhosis could show broader clinical activity, providing a potential regulatory path to approval as the first FDA-approved therapy in liver cirrhosis. We may also consider further development of GB1211 in hepatocellular cancer, which often occurs in patients with cirrhosis of any etiology, where a product that is administered orally and has a favorable tolerability profile could offer significant advantages over current treatment options.

Oncology Indications

Our initial target indication for GB1211 in oncology is NSCLC, a cancer indication with a high unmet medical need despite recent medical progress with checkpoint inhibitor therapies. Many tumors overexpress galectin-3, which mechanistically is linked to several cancer promoting mechanisms, including those linked to programmed cell death receptor 1 (PD-1) or its ligand, PD-L1 resistance and chemotherapy resistance, and may ultimately lead to worse clinical outcomes. Galectin-3 inhibition has the potential to both directly reduce tumor growth as well as increase the immune mediated eradication of tumors and is believed to increase T-cell recruitment and activation in the tumor microenvironment. We believe that inhibiting galectin-3 could lead to an increase in the efficacy of checkpoint inhibitors in cancer patients, and especially those with galectin-3 expression. In an animal model, we observed that oral administration of our galectin-3 inhibitors reduced human and mouse lung adenocarcinoma growth and blocked metastasis. Treatment with one of our galectin-3 inhibitors also potentiated the activity of a PD-L1 immune checkpoint inhibitor. The mechanisms at work include checkpoint inhibitor-type mechanisms (inhibition of TGF-β signaling, LAG-3, T-cell receptor, interferon gamma) and mechanisms potentially enhancing PD-1/PD-L1 activity, as evidenced by preclinical data that we recently presented at the 2022 American Society of Clinical Oncology Annual Meeting showing that GB1211 reversed a galectin-3 induced blockage of the checkpoint inhibitors atezolizumab and pembrolizumab and exhibited synergistic effects with these checkpoint inhibitors. Furthermore, in the clinic, a retrospective study showed that patients with high tumor staining for galectin-3 were resistant to treatment with pembrolizumab, an anti-PD-1 antibody approved for the treatment of NSCLC, and, by contrast, patients with low galectin-3 had a good response to pembrolizumab and a reduction in tumor volume. Recent clinical data has shown clinical activity when using a LAG-3 inhibitor in combination with a PD-1 inhibitor. We believe galectin-3 is a principal activator of LAG-3 and mediates LAG-3 effects, and in preclinical studies we have shown that GB1211 can block galectin-3 binding to LAG-3, in addition to other galectin-3 cancer promoting mechanisms. Thus, galectin-3 could be a biomarker for anti-PD-1/PD-L1 resistance and, therefore, also be a marker for patients who may benefit from galectin-3 inhibition, which could enable a biomarker-based therapy. We believe the emerging data of galectin-3 as a checkpoint inhibitor resistance mechanism supports a key role for our oral galectin-3 inhibitor candidates in cancer therapy.

In the fourth quarter of 2021, we announced that we had entered into a clinical trial supply agreement with Roche for our Phase 2a GALLANT-1 trial of GB1211 in combination with atezolizumab, a PD-L1 checkpoint inhibitor, for the treatment of first-line NSCLC. This randomized, double blind, placebo-controlled trial is examining the effect of GB1211 and atezolizumab on tumor shrinkage based on RECIST criteria, as well as secondary endpoint measures such as overall survival, progression-free survival and others. We also plan to analyze how plasma galectin-3 levels and tumor galectin-3 correlate with tumor response. We initiated Part A of this trial, an open-label study to select the dose of GB1211 to be used with atezolizumab, in the second quarter of 2022. In the first 6 patients who received 200mg twice daily in combination with atezolizumab, we observed two serious adverse events of autoimmune-type skin rashes (showing perivascular lymphocytic infiltrates), which were determined by the principal investigator to be related to the administration of atezolizumab. The reactions were similar to those observed with atezolizumab and described in the label. Both reactions responded to therapy with oral glucocorticosteroids and were clinically manageable. In accordance with the protocol, we reduced the GB1211 dose to 100mg twice daily for the second patient cohort. Recruitment in this cohort is currently ongoing. Interestingly, inflammatory and perivascular lymphocytic infiltrates were observed in both skin reactions, and could signal an exaggerated immune activation, something often observed with checkpoint inhibitor therapy and associated with improved clinical outcomes. Because a central aspect of the mechanism of action for GB1211 in combination with a checkpoint inhibitor is to remove galectin-3 from the lymphocytes and the tumor cells, and thereby increase lymphocyte-based tumor killing, we believe this could also be a positive signal of enhanced lymphocyte activation. We expect to release interim safety data from this part of the GALLANT-1 trial in the second quarter of 2023. Part B of this trial is designed to evaluate the safety and tumor shrinkage (based on RECIST criteria) of the combination of the selected dose of GB1211 and atezolizumab and we expect topline results to be available in the first half of 2024.

In October 2022, we expanded our focus on additional oncology indications and entered into an agreement with Providence Portland Medical Center's EACRI to evaluate the safety and efficacy of GB1211 in combination with pembrolizumab in an investigator-initiated trial in metastatic melanoma and HNSCC patients. Galecto has committed to supply GB1211 for this Phase 2 trial. The randomized, double-blind placebo controlled, investigator-initiated Phase 2 trial is expected to evaluate whether the addition of GB1211 increases the response rate of pembrolizumab in metastatic melanoma and HNSCC patients. The study is designed to evaluate GB1211 in combination with the standard therapeutic dose of pembrolizumab in patients with unresectable or metastatic melanoma or recurrent or metastatic HNSCC progressing during or after platinum-containing chemotherapy. In addition to monitoring for toxicity and clinical response, blood and tumor samples will be obtained to assess immunologic measures

relevant to galectin-3 biology and checkpoint inhibition. This trial is expected to begin in the second half of 2023 and topline results could be reported as early as 2025.

Organizational Background

We are built upon more than a decade of research into galectin, fibrosis and cancer modulators and were founded by leading researchers on the galectin family of proteins, including one of the discoverers of the galectin family of proteins, the first chemist to develop selective galectin inhibitors based on the x-ray crystal structure of galectin-3, and the discoverer of galectin-3's role in fibrosis and cancer. We believe we were the first company to apply click-chemistry in the galectin field and the first to synthesize highly potent small molecule inhibitors of galectin-3. Our founders, executives and employees have significant experience that provides unique insights into the targets that underlie the biological process of fibrosis, cancer and other related disease. We leverage this expertise, as well as established relationships with outside consultants and universities, to achieve cost-effective and efficient drug development. We have developed from a university spin-out, with only one part-time employee at inception in December 2011, to a company with three product candidates in Phase 2 clinical development and several preclinical molecules with differentiated specificity advancing towards the clinic.

Our Strategy

Our goal is to become a leader in developing and commercializing therapeutics that directly target the biological processes at the heart of fibrotic diseases and cancer. Our strategy is focused on the following key components:

- **Efficient advancement of GB0139 in IPF through clinical development**. We are currently conducting a Phase 2b trial of GB0139 in patients with IPF, with topline data expected in mid-2023. IPF is an orphan disease that is therapeutically underserved, and we believe that GB0139 may have the ability to become the first true disease-modifying therapy. Assuming positive results from the Phase 2b trial, we intend to expeditiously initiate a Phase 3 trial program in IPF.

- **Further develop GB1211 for the treatment of liver disease.** There remains a significant need for disease-modifying therapies that postpone or replace liver transplantation in late-stage liver cirrhosis patients. In the fourth quarter of 2022, we announced topline results from our Phase 1b/2a GULLIVER-2 trial in patients with decompensated liver cirrhosis showing statistically significant reductions in ALT ($p<0.0005$), AST ($p<0.005$) and GGT ($p<0.05$), with encouraging reductions for ALP ($p<0.09$), after 12 weeks of treatment. These findings suggest that GB1211 provided liver cell protection and improved liver status, further supporting clinical development in severe liver disease. The consistency of the changes and the progressive improvement, together with the favorable safety profile, observed in this trial lead us to believe that a broader study in patients with compensated and/or decompensated cirrhosis could show wider effects, providing a potential regulatory path as the first FDA-approved therapy for liver cirrhosis. Our next step in the development of GB1211 for the treatment of liver cirrhosis and other liver diseases is to conduct a Phase 2b trial, subject to obtaining additional financing or collaborating with a third party. We may also consider further development of GB1211 in hepatocellular cancer, which often occurs in patients with cirrhosis of any etiology, where a product that is administered orally and has a favorable tolerability profile could offer significant advantages over current treatment options.

- **Build on our understanding of the galectin-3 target to develop our pipeline of oncology product candidates.** Galectin-3 has been identified as the guardian of the tumor microenvironment, driving cancer growth and allowing tumor cells to escape the immune mediated attack through the activation of a number of central tumor-promoting mechanisms such as LAG-3, TGF-β, VEGF and K-Ras. Galectin-3 inhibition has the potential to both directly reduce tumor growth and increase the immune-mediated eradication of tumors. Galectin-3 inhibition is believed to increase T-cell recruitment and activation in the tumor microenvironment, as well as increase the efficacy of checkpoint inhibitors in cancer patients with high galectin-3 expression. We are collaborating with (i) Roche in the examination of GB1211 combined with atezolizumab for the first-line treatment of NSCLC and (ii) Providence Portland Medical Center in the examination of GB1211 with pembrolizumab for the treatment of melanoma and HNSCC. However, we also believe that GB1211 has the potential to treat many other forms of cancer and we plan to conduct additional oncology trails in the future, subject to obtaining additional financing or collaborating with a third party.

- **Leverage our understanding of the LOXL2 pathway to advance GB2064 through a Phase 2 trial in myelofibrosis and continue evaluating GB2064 in subsequent indications.** We are currently conducting a Phase 2 trial of GB2064, our lead product candidate targeting LOXL2, in myelofibrosis. In the third quarter of 2022, we announced that of the first five patients who had completed at least six months of treatment with GB2064 and had a valid bone marrow biopsy at baseline and at 6 months in our Phase 2a MYLOX-1 trial, four experienced a ≥ 1-grade reduction in collagen fibrosis of the bone marrow, an improvement suggesting that GB2064 could impact the progression of the disease and potentially be disease modifying. The data from the planned intermediate assessment of the MYLOX-1 trial suggest that the LOXL2 mechanism may be a way to reduce bone marrow fibrosis, which we believe has not been shown with any FDA-approved therapy. We continue to enroll patients in the MYLOX-1 trial and expect topline results from the MYLOX-1 trial to be available by the end of 2023. Because the MYLOX-1 trial has already exceeded the pre-defined target of a ≥ 1 grade reduction in collagen fibrosis in at least three patients, we may determine to enroll fewer patients than the sixteen evaluable patients provided for in the protocol. We are also beginning to plan for next steps in clinical development, which we expect could include combining GB2064 with another myelofibrosis treatment. The data from the intermediate assessment and the published literature on the LOXL2 mechanism suggest that LOXL2 inhibition may also be important in other solid and liquid tumor types as well as in fibrotic diseases.

- **Continue to build a patient-focused company targeting fibrosis and cancer.** In building a patient-focused company to address the needs of patients with fibrotic diseases and cancer, we are working with clinicians, patient advocacy groups, medical centers of excellence and medical key opinion leaders to better understand unmet medical needs, to expeditiously develop and provide better treatments to patients, and to increase awareness of these diseases.

- **Expand our fibrosis and cancer portfolio by opportunistically advancing our research and development efforts beyond our current expertise in the galectin and LOXL2 pathways.** We intend to expand our leadership as a company dedicated to developing therapies that directly target the biological processes at the heart of fibrotic diseases and cancer by developing product candidates against other targets involved in the regulation, formation, or maintenance of fibrosis or cancer. We also intend to selectively pursue business development opportunities to expand our current product portfolio, which may include product candidates targeting fibrosis or cancer that work through mechanisms that we believe are complimentary to, or independent of, galectins or LOXL2.

- **Maximize the commercial value of our product candidates.** We have retained worldwide development and commercial rights to all of our product candidates. We intend to commercialize any products in our portfolio for which we receive regulatory approvals in certain rare indications in the United States and the EU with a limited and targeted commercial team. We also intend to retain the flexibility to evaluate strategic collaborations and to seek partners to commercialize our products in other geographies and for our products in highly prevalent indications such as NSCLC, which require significant investment to build a commercial infrastructure. We have built an extensive wholly-owned patent portfolio around our fibrosis and oncology pipeline. We intend to continue to seek additional patent protection as we develop additional novel fibrosis and oncology candidates using our existing galectin and LOXL2 experience.

Galectin-3 and LOXL2 Mediated Fibrosis and Cancer Background

We are developing small molecule inhibitors focusing on galectin-3 and LOXL2 that target key common cellular and molecular biological processes that drive fibrosis and cancer and have shown antifibrotic and anticancer activity *in vivo*. High levels of galectin-3 and LOXL2 are linked to worse clinical outcomes in both fibrosis and many types of cancer.

Fibrosis is the development of abnormal fibrous connective tissue in response to injury, damage or dysfunctional gene regulation. This fibrous connective tissue consists of elongated proteins such as collagen and elastin fibers that provide support to surrounding key functional cells in all tissue and all organs. Production and break-down of collagen is tightly regulated to preserve optimal organ function. The deposition of excess collagen and the formation of fibrosis can cause remodeling of surrounding healthy tissue and the loss of normal organ or tissue function. Fibrotic disease can affect tissues throughout the body including the lungs, liver, heart, kidneys and vascular system. Fibrosis typically progresses slowly and can ultimately lead to organ failure and death. Fibrosis is also a hallmark of solid tumors, with up to 20 percent of cancers associated with chronic inflammation-linked fibrosis. It has been estimated that fibrosis contributes to up to 45 percent of all deaths in the developed world.

The currently approved therapeutic treatments for IPF are associated with significant side effects leading to significant discontinuation rates with median time on treatment only between 7.5 and 8.9 months, and they have not been linked to improvements in overall survival. Scientific literature supports the understanding that there are common biological mechanisms that drive fibrosis that are distinct from those regulating inflammation. It is these mechanisms that we are targeting with our proprietary product candidates.

Both LOXL2 and galectin-3 have been shown to also play central roles in cancer progression and the formation of fibrosis associated with the tumor and in the tumor microenvironment (TME). These effects help tumors grow, metastasize and evade anticancer treatments. Hence, by inhibiting LOXL2 and galectin-3, it may be possible to reduce tumor growth, enhance the effect of anticancer treatments and hence reduce disease progression and potentially improve survival.

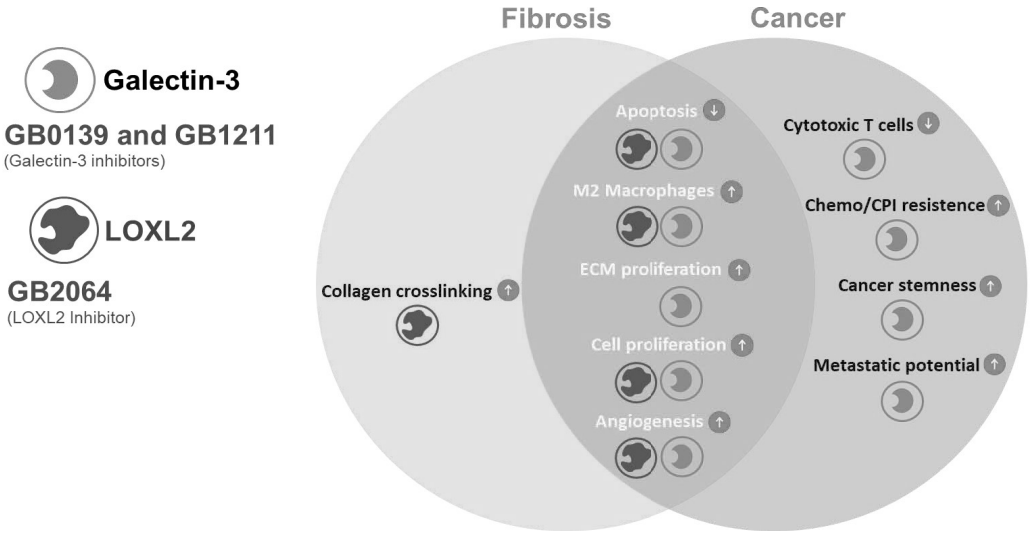


Figure 2. Overlapping biology in fibrosis and cancer through galectin-3 and LOXL2

Galectin-3

Galectin-3 is a lectin central to the development of fibrotic disease across multiple tissue types and is part of a pre-innate galectin immune defense developmentally conserved for over 500 million years, which steers local inflammation and when chronically activated, drives the development of fibrosis via several pathways and several cell inflammatory cell types and fibrocytes.

There is very little expression of galectin-3 in healthy tissues, but galectin-3 is overexpressed, sometimes profoundly, in damaged or inflamed tissues. Galectin-3 drives fibrosis by activating multiple pathways involved in tissue injury and repair. The presence of excess galectin-3 triggers the fibrotic process by converting quiescent fibroblast cells into activated cells called myofibroblasts. This triggering effect takes place when galectin-3 stimulates the signaling of growth factor receptors such as TGF-β, a master regulator of cell growth, immune regulation and fibrosis. Myofibroblasts are harmful in the context of fibrosis, since they secrete excess collagen and elastin, and as such are the key cellular drivers of fibrosis. Furthermore, galectin-3 reduces apoptosis, or programmed cell death, of inflammatory cells called neutrophils, allowing these cells to persist and potentially cause further damage and abnormal repair in fibrotic tissue. Finally, galectin-3 also promotes the activation of macrophages, resulting in increased fibrosis as well as further galectin-3 expression, which leads to a feed-forward cycle that can accelerate the fibrotic process.

The galectin-3 mediated fibrosis is central to IPF and to several cancer types. The galectin-3 inhibitors inhibit the carbohydrate recognition domain stopping the attachment of galectin-3 to sugar moieties on cell surfaces receptors, and therefore stops its activation of key molecules like the receptors for TGF-β and VEGF. Given its central role in fibrosis, there are FDA- and EU-cleared diagnostics for the detection of galectin-3 used for assessing the prognosis of patients diagnosed with chronic heart failure.

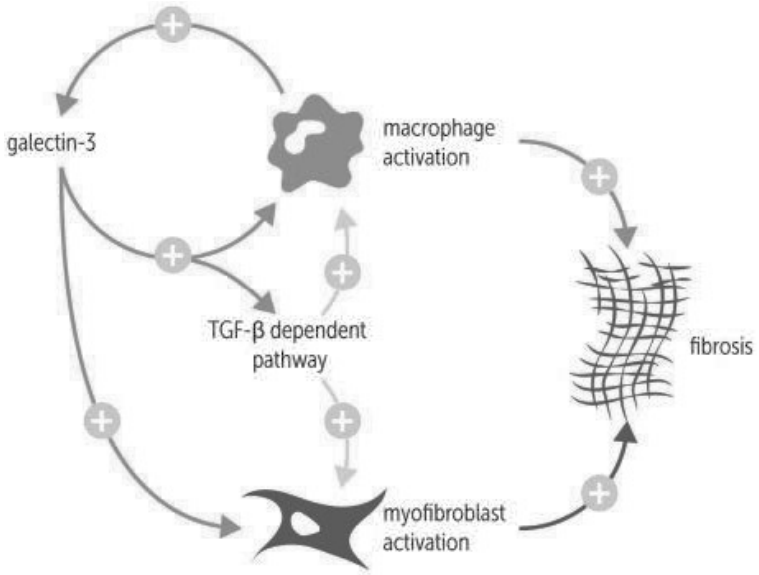


Figure 3. Multiple roles of galectin-3 in fibrosis

Interestingly, studies have shown that galectin-3 is not expressed during the first trimester of pregnancy and intra-uterine surgery during this time period leaves no scars. The inability of first trimester fetuses to scar further demonstrates that fibrotic tissue cannot develop if galectin-3 is missing or blocked. Preclinical studies have also shown that mice deficient in galectin-3 exhibit decreased fibrosis in models of liver, kidney, and lung disease. Furthermore, inhibition of galectin-3 has been shown to slow the development of lung, liver and cardiac fibrosis in preclinical models.

In patients with IPF, elevated galectin-3 is found in the fibrotic patches in the lung, in bronchoalveolar lavage, or BAL, fluid and in plasma. In longitudinal studies, elevated galectin-3 has been associated with a greater decline in lung function. Patients with liver cirrhosis have highly elevated galectin-3 levels in biopsies of their liver nodules. Elevated galectin-3 is also found in serum of patients with fibrosis related to diseases characterized by fibrosis such as cancer, cardiac disease and renal disease. The level of galectin-3 expression in fibrotic tissue both spatially and temporally correlates with the degree of fibrosis.

Despite galectin-3's proximity to and involvement in fibrosis disease pathology, no approved drugs specifically target galectin-3. However, there are FDA- and EU-cleared diagnostics for the detection of galectin-3 in plasma to assess the prognosis of patients diagnosed with chronic heart failure.

Galectin-3 is widely expressed in several cell types such as macrophages, fibroblasts, activated T-lymphocytes and epithelial cells and is highly expressed in high fatality cancers such as NSCLC. In NSCLC, particularly in adenocarcinoma, increased galectin-3 expression in tumors, lymph nodes and serum correlate with metastases and is a negative prognostic indicator. The galectin-3 genetic polymorphism rs4652 associated with impaired galectin-3 secretion has been linked to increased survival and response to chemotherapy in NSCLC. Galectin-3 drives fibrosis and blocking fibrosis around cancers may improve responses to immunotherapy and chemotherapy, as well as reduce angiogenesis and metastasis. Galectin-3 can directly enhance cell proliferation, apoptosis resistance and metastatic potential, as well as lung cancer stemness. It is also an important constituent of the tumor microenvironment acting on endothelial cells to promote angiogenesis and blocking galectin-3 inhibits angiogenesis. Ras mutations are the most common oncogenic driver mutation in human cancers and Ras mutations are dependent galectin-3 to drive oncogenic signaling. Thus, galectin-3 inhibitors could be effective in blocking oncogenic signaling in human tumors with Ras mutations, such as NSCLC, colorectal cancer and pancreatic cancer. Furthermore, many studies have revealed the inhibitory effects of galectin-3 on activated cytotoxic T lymphocytes (CTLs), and we have shown in preclinical trials that it is essential for M2 macrophage differentiation. In a recent study it was shown that patients with high levels of galectin-3 expression in NSCLC tumors did not respond to anti-PD-1 treatment, whereas patients with lower levels of galectin-3 expression did respond to the treatment. Similar data was also seen in melanoma patients, suggesting that the inhibition of galectin-3 may be broadly applicable in a number of cancers and indicating a central role of galectin-3 in the tumor defense mechanisms. Recent clinical data has shown clinical activity using a LAG-3 inhibitor in combination with a PD-1 inhibitor. Galectin-3 is a principal activator of LAG-3 and mediates LAG-3 effects.

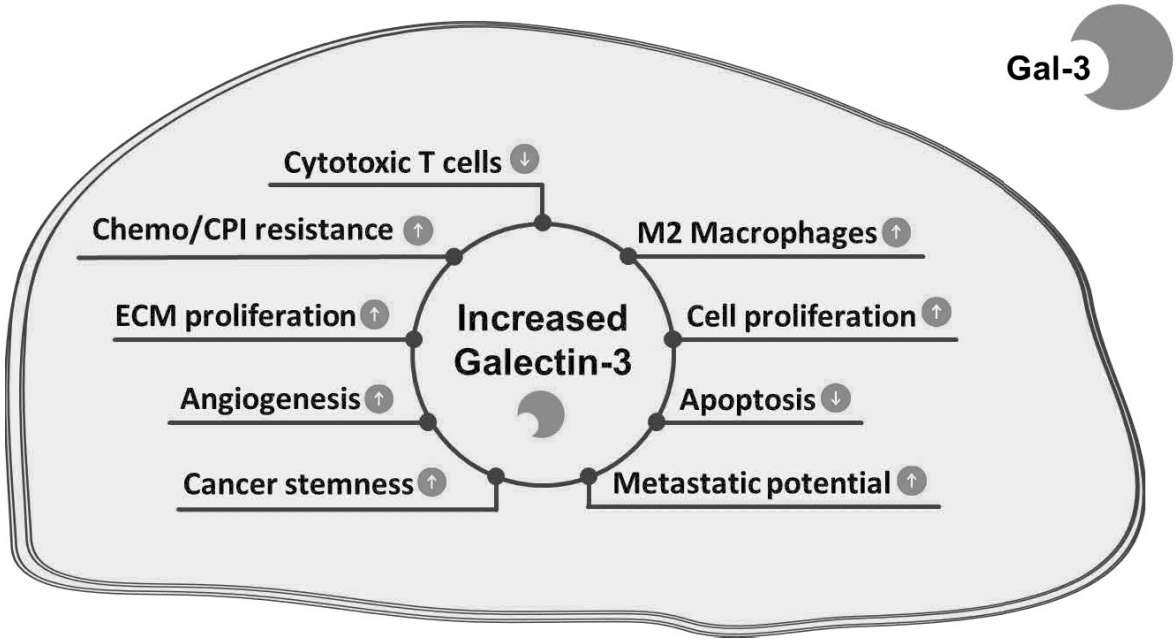


Figure 4. Increased levels of tumor galectin-3 significantly drives the hallmarks of cancer

LOXL2

Lysyl oxidases are a family of enzymes that are secreted from the cell. Once outside the cell membrane, these enzymes help create and strengthen connective tissue by catalyzing the crosslinking of proteins such as collagen and elastin in the extracellular matrix, which is essential for normal tissue function, but can become fibrotic and lead to organ dysfunction in the diseased state. There are five members of the LOX family in humans, LOX and LOXL1 through LOXL4. Each of these family members is believed to play a specific role in the formation and maintenance of the extracellular matrix. Any therapy that is not sufficiently specific to LOXL2 (i.e., that also interacts with other members of the LOX family) is at risk for creating toxicity. Mice deficient in the gene for LOX, for example, die soon after birth as a result of defects in the formation of the cardiovascular and respiratory systems.

We have chosen to target only the LOXL2 enzyme because it plays a key role in the development of fibrosis. In fibrotic diseases such as lung, liver, and kidney fibrosis, increased levels of LOXL2 are observed. The level of LOXL2 expression correlates with the degree of liver fibrosis, with the highest levels of LOXL2 being found in cirrhosis and in decompensated liver disease.

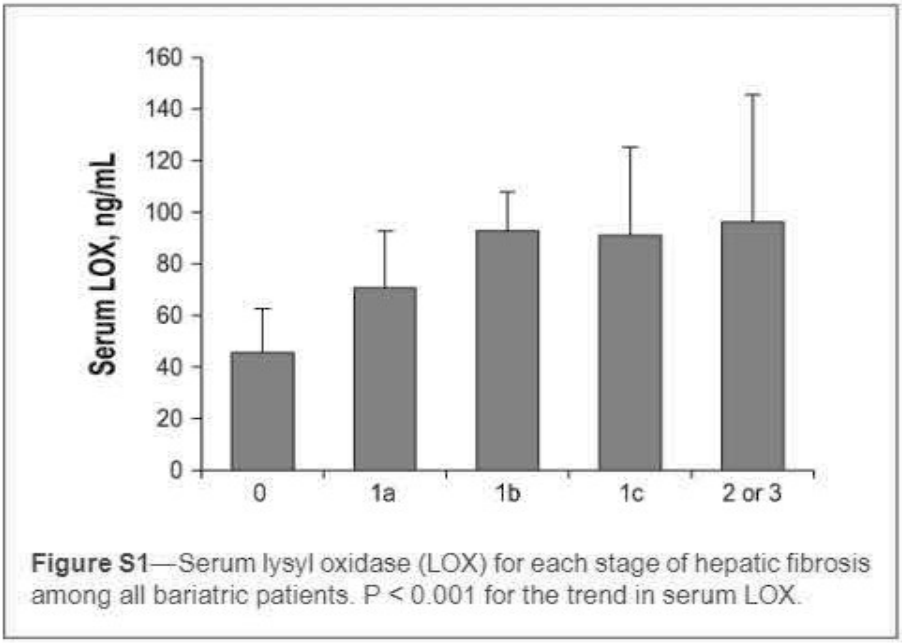


Figure 5. LOXL2 expression correlates with degree of liver damage in patients with chronic hepatitis B

LOXL2 is also increased in cancer-related fibrosis across a wide range of cancers, including breast, colon, and pancreatic cancers. The presence of LOXL2 is a negative prognostic for survival in pancreatic cancer with patients with tumors expressing LOXL2 having an overall survival of approximately half of those with LOXL2 negative tumors. LOXL2 is significantly upregulated in mesenchymal stromal cells, which are bone marrow cells that support hematopoietic stem cell differentiation, isolated from patients with myelofibrosis compared to healthy adults. The levels of other LOX family members do not significantly change between healthy and diseased mesenchymal stromal cells.

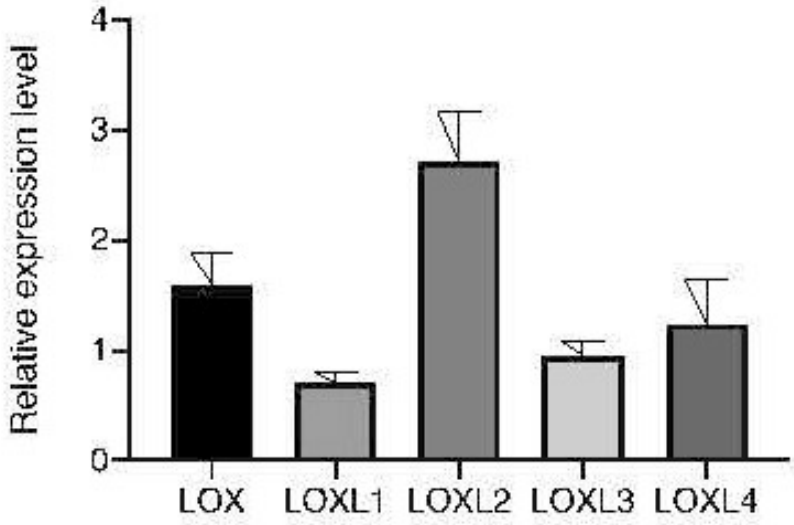


Figure 6. LOXL2 is highly overexpressed in myelofibrosis stromal cells (expression level in myeloid biopsies from myelofibrosis patients relative to expression in healthy individuals)

Clinical experience with drugs specifically targeting LOXL2 has been limited. Simtuzumab, an antibody targeting LOXL2 that is administered by a subcutaneous or intravenous injection, has been evaluated in a number of clinical trials, including a Phase 2b trial in patients with myelofibrosis. These trials failed to show a positive effect on the reduction of fibrosis and further development of simtuzumab was discontinued due to lack of efficacy. Simtuzumab binds to LOXL2 without fully inhibiting its catalytic activity. This activity is, we believe, the critical feature of LOXL2 that needs to be blocked in order to achieve maximal antifibrotic activity. We believe that the LOXL2 target has not been fully explored. There is evidence that small molecule inhibitors with high penetration through fibrotic tissue that directly inhibit the catalytic activity of LOXL2 and which have the ability to penetrate deeper into fibrotic tissue than a large molecule antibody may show greater activity as antifibrotic agents, given that small molecules can more readily bind to the catalytic site of an enzyme deep in fibrotic tissue. GB2064 is designed to inhibit the enzymatic center to a much higher degree than simtuzumab and shut down collagen cross-linking more effectively. Inhibitors that preferentially target LOXL2 over other LOX family members may avoid triggering adverse events due to the ubiquitous and important roles that lysyl oxidases have in maintaining tissue structure throughout the body.

Our Clinical Product Candidate Portfolio

GB0139 for the Treatment of IPF

GB0139 is an inhaled small molecule inhibitor of galectin-3 that we are developing for the treatment of IPF. GB0139 has been tested in toxicological studies and observed to have a favorable tolerability profile in chronic toxicity studies. The molecule is delivered via oral inhalation utilizing a dry powder inhaler, a standard capsule-based inhaler that has been previously approved by the FDA for use in the delivery of other compounds. GB0139 for the treatment of IPF has been granted orphan drug designation by both U.S. and European regulatory authorities.

IPF Background and Market Opportunity

IPF is a rare life-threatening disease characterized by progressive fibrosis of the lungs leading to their deterioration and destruction. The most common symptoms of IPF are shortness of breath and a dry persistent cough, and a decreasing ability to perform normal daily activities. Over time, as a result of the unrelenting progress of the disease, breathing difficulties increase and lack of oxygen to tissues triggers weight loss, aching muscles, chronic fatigue, generally deteriorating health and can ultimately lead to death, often within 2 to 5 years.

IPF is a rare disease affecting approximately 100,000 people in the United States and occurs primarily in persons between the ages of 50 and 70. Between 30,000 and 40,000 new cases are diagnosed in the United States each year. The exact cause of IPF is not known, but a family history of the disease and environmental exposure to toxins, such as smoking, are known to increase the likelihood of developing the disease. Some patients with IPF develop other serious lung conditions such as lung cancer, pulmonary embolisms, pneumonia and pulmonary hypertension. Patients with IPF generally have a poor prognosis with a mean survival between two to five years depending on the stage of diagnosis and the rate of lung deterioration.

Current Treatments for IPF and Their Limitations

Some IPF patients with mild or moderate symptoms are treated with either nintedanib, marketed as Ofev® by Boehringer Ingelheim, or pirfenidone, marketed as Esbriet® by Roche/Genentech. These drugs have been shown to slow progression of decrease in lung function associated with IPF and deterioration of pulmonary function, but neither drug has been associated with improvements in overall survival, and both have been associated with significant side effects. Over 60 percent of patients dosed with nintedanib have diarrhea and 14 percent experience elevated levels of liver enzymes. Thirty percent of patients treated with pirfenidone have skin rash, and nine percent experience photosensitivity, both of which can lead to dose reductions or discontinuations. Both agents have some efficacy in patients with more advanced disease, but high rates of discontinuations due to adverse events in these patients limit their use. The median time on treatment for currently approved therapies is only between 7.5 and 8.9 months, and these treatments have not been linked to improvements in overall survival. A survey of 290 physicians published by a third party in 2017 found that over half of IPF patients are not being treated with either agent for multiple reasons, including physicians not having sufficient confidence in clinical benefit and concerns about safety. A retrospective cohort analysis of prescription records conducted by researchers at the Mayo Clinic and presented in 2019 found that the adoption of pirfenidone and nintedanib by IPF patients was approximately ten percent for each therapy, supporting the earlier observation that the majority of IPF patients are not actively being treated. Despite this, total worldwide sales of pirfenidone and nintedanib combined were approximately $3.7 billion and $3.5 billion in 2021 and 2020, respectively.

Given the poor prognosis and the lack of therapies that impact survival, patients diagnosed with IPF are routinely referred for lung transplantations and it is generally recommended that all patients without contraindications for surgery be added to transplant lists. IPF patients represent the majority of all lung transplantations. However, the survival rate of IPF patients following transplant is lower than that observed for other diseases due to their advanced age and associated comorbidities.

Our Solution - GB0139

We are developing GB0139 for inhaled delivery to target the IPF disease site directly in the periphery of the lung while limiting potential systemic toxicity. GB0139 is differentiated from current IPF therapies because it is designed to directly target galectin-3. By inhibiting the carbohydrate binding domain of galectin-3, GB0139 is designed to prevent the binding of galectin-3 to cell surface receptors, and hence reduce the profibrotic activity of galectin-3. GB0139 has been generally well-tolerated in clinical trials we have completed to date both in healthy adults and in IPF patients. In both populations, dosing with GB0139 resulted in highly consistent drug exposure and led to reductions in galectin-3 levels in macrophages isolated by BAL in the IPF patients. In our Phase 2a clinical trial, local therapy in the lungs of IPF patients with GB0139 also led to markedly decreased systemic levels of plasma biomarkers, such as YKL-40 and PDGF, that have been linked to mortality, severity and/or progression in IPF. While we are currently developing GB0139 for the treatment of IPF, we also plan to further develop GB0139 with the goal of treating other severe lung diseases driven by galectin-3.

GB0139 has also been investigated in a Phase 2a DEFINE trial as part of the University of Edinburgh's rapid experimental program for COVID-19 respiratory failure. We believe that GB0139's mechanism of action suggests it may have potential to prevent infection with COVID-19, as well as treat cytokine release syndrome, one of the major complications of the infection that can cause long-term damage in the lungs. This DEFINE trial included 41 hospitalized patients with COVID-19 infection who did not require mechanical ventilation, of which 20 were randomized to the GB0139 plus standard of care (dexamethasone, remdesivir and anticoagulant therapy) arm. The trial met its primary endpoint with results showing that inhaled GB0139 had an acceptable tolerability profile when used in combination with standard of care in hospitalized patients with COVID-19 pneumonia. Despite being breathless and requiring oxygen, patients receiving GB0139 plus standard of care were able to inhale and achieve consistent exposure of GB0139. The 10mg dose of GB0139, dosed twice a day for 2 days and subsequently once a day for up to 14 days, which was higher than the current 3mg dose being used in the ongoing GALACTIC-1 trial, was generally well-tolerated and no treatment-related serious adverse events were reported. Furthermore, inhaled GB0139 led to a significant reduction of galectin-3 levels in patients with COVID-19 compared to standard of care (dexamethasone, remdesivir and anticoagulant therapy), demonstrating target engagement and reduced plasma levels of other key biomarkers associated with severe disease and a poor prognosis, including YKL-40, PAI-1, CXCL10, IL-6, IL-10 and TNFα. Patients receiving GB0139 also showed improved inflammation and coagulation biomarkers, including CXCL10, thrombocytes and reduced D-dimers, as well as improved biomarkers of liver function and tissue damage.

COVID-19 pneumonitis is very fibrotic and, in some cases, can lead to "long COVID" lung fibrosis. COVID-19 patients treated with GB0139 showed a reduction in the processes and biomarkers of acute and chronic fibrosis. These results represent additional evidence of the positive impact of galectin-3 inhibition in severe lung disease, strengthening our confidence in the potential safety and tolerability profile of GB0139 in patients with compromised lung function and indicating potential activity in virus-induced acute lung injury. Viral infection and features of acute lung injury are associated with acute exacerbations of IPF, a major cause of rapid decline in lung function and death. The results from this study aligned with our findings in our IPF clinical trials and reaffirms the potential efficacy of GB0139 in IPF our ongoing Phase 2b GALACTIC-1 trial and also the potential to reduce acute exacerbations. We plan to continue to explore co-development opportunities with GB0139 for the treatment of COVID-19 and other severe viral lung diseases.

Overview of Clinical Trials

Data from our completed clinical trials to date on GB0139 in IPF patients demonstrated that:

- High exposure of GB0139 can be delivered to the target tissue with low systemic exposure;
- Inhalation dosing of IPF patients is feasible and results in highly reproducible drug levels;
- GB0139 was generally well-tolerated, including daily dosing;
- GB0139 leads to dose-dependent decreases in galectin-3 levels; and
- GB0139 leads to decreases in multiple fibrosis biomarkers that are present in the diseased lung tissue and measured in plasma, including YKL-40 and PDGF, which is consistent with GB0139 having direct antifibrotic activity.

Ongoing Phase 2b Clinical Trial – GALACTIC-1 Trial

In March 2019, we initiated the GALACTIC-1 trial, a 52-week randomized, double-blind, multicenter, parallel, placebo-controlled Phase 2b trial investigating the safety and efficacy of GB0139 in patients with IPF. The primary endpoint is the annual rate of decline in FVC at one year. FVC is a common test that measures the total amount of air that a person can expel from the lungs. A decline in FVC is an indirect measure of worsening fibrosis and increased lung stiffness and has become the most commonly accepted measure of disease progression in IPF. Patients with IPF lose FVC at a higher rate than normal leading to invalidity and, ultimately, to death. Therefore, a reduction in decline of FVC is the endpoint that was accepted by the FDA for the approval of both pirfenidone and nintedanib, the two current therapeutic treatments for IPF.

In the clinical Phase 1b/2a study, both the 3 and the 10mg dose were shown to reach the periphery of the lung at high concentrations and to reduce the extracellular levels of galectin-3 on alveolar macrophages harvested from the lung of IPF patients. In the current clinical trial design for the GALACTIC-1 trial, patients are receiving an inhaled daily dose of 3mg of GB0139 or placebo for one year. In March 2021, the DSMB, who had access to unblinded interim safety and efficacy data, recommended that we discontinue dosing of GB0139 in patients on nintedanib or pirfenidone, and in patients receiving the 10mg dose. The DSMB's determination was based on an identification of an imbalance in the serious adverse events across the study groups, but not an imbalance between the groups in mortality. During the second quarter of 2021, we amended the study protocol to reflect these changes, and in July 2021, we resumed recruitment of patients for the GALACTIC-1 trial with the 3mg dose. Since July 2021, the DSMB has reviewed the unblinded safety data multiple times and has not communicated to us any safety signals or recommended any changes in the protocol. As with the initial study design, the annual rate of decline in FVC will be assessed as the primary endpoint using baseline FVC and several FVC measurements during the year to establish the rate of decline, and to compare that measure between patients on active treatment versus placebo. Secondary endpoints include the absolute decline in FVC; time to first hospitalization related to IPF, including acute IPF exacerbation; overall survival; and patient outcome measures such as 6-minute walk test distance and quality of life as determined by standard instruments. All patients will continue receiving their blinded treatments for up to two years until the last patient completes one year of dosing enabling the generation of extended safety and efficacy data.

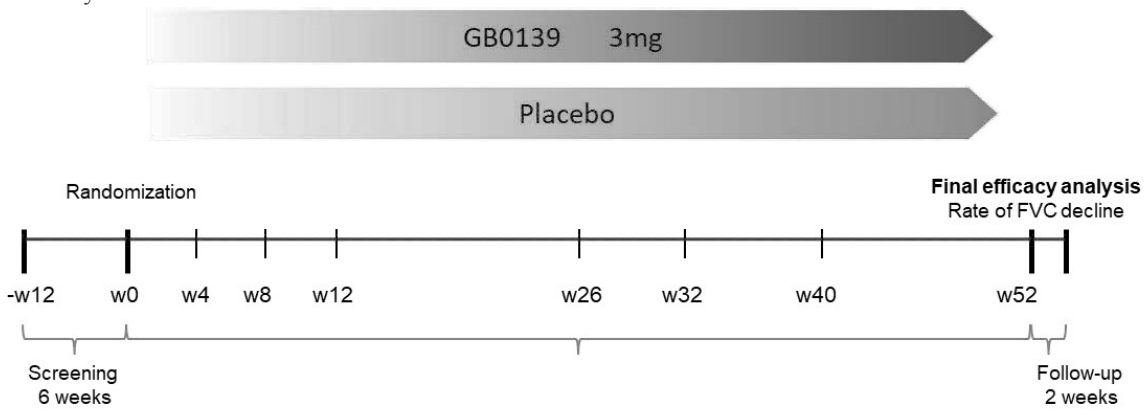


Figure 7. Ongoing GALACTIC-1 trial design

The table below shows an overview of the interim blinded safety data in the study. As the data has not been fully cleaned, since the study is ongoing, this table should not be seen as the final and definitive adverse event table, but is included here to provide an impression of the character of the serious adverse events that have been reported in the study as treatment emergent (i.e. starting after the onset of dosing of the experimental drug inhalations). Since the table represents a blend of patients on placebo, the 3mg dose of GB0139 and the 10mg dose of GB0139, including those taking concomitant nintedanib and pirfenidone, no firm conclusion can be made that these reported serious treatment emergent adverse events are related to GB0139 and conversely neither that they are unrelated to the GB0139 therapy.

System Organ Class/Preferred Term	Patients on nintedanib or pirfenidone N=193			Patients NOT on nintedanib or pirfenidone N=85		
	n	%	SAEs	n	%	SAEs
Subjects with at least one serious adverse event (SAE)	38	19.7	59	9	10.6	13
Respiratory, thoracic and mediastinal disorders	21	10.9	24	5	5.9	6
Infections and infestations	14	7.3	17	4	4.7	5
General disorders and administration site conditions	4	2.1	4	1	1.2	1
Cardiac disorders	4	2.1	5	0	0	0
Blood and lymphatic system disorders	2	1.0	2	0	0	0
Hepatobiliary disorders	0	0	0	1	1.2	1
Injury, poisoning and procedural complications	1	0.5	1	0	0	0
Neoplasms benign, malignant and unspecified (e.g., cysts and polyps)	1	0.5	2	0	0	0
Nervous system disorders	1	0.5	1	0	0	0
Skin and subcutaneous tissue disorders	1	0.5	1	0	0	0
Uncoded	1	0.5	1	0	0	0
Vascular disorders	1	0.5	1	0	0	0

Figure 8. GALACTIC-1 Interim blinded safety data as of March 2021

Completed Phase 1/2a Clinical Trial - Phase 2a Part in IPF Patients

We have conducted a randomized placebo-controlled Phase 1/2a multi-dose trial of GB0139 in the United Kingdom, or U.K., with the Phase 2a part conducted in 24 IPF patients. Patients in this part received 0.3, 3, or 10mg of GB0139 or placebo control by inhalation once daily for 14 days. All patients completed the 14-day dosing and BAL samples were obtained for all patients before dosing and at the conclusion of dosing.

GB0139 was generally well-tolerated in these patients with no serious drug-related adverse events, and there were no discontinuations in the trial. There were four incidents of mild adverse events (fever, upper respiratory tract infection, abnormal taste in mouth and dry throat) that were deemed possibly or probably drug related.

Despite the presence of lung damage from IPF in patients entering this trial, inhalation of GB0139 resulted in highly reproducible drug levels (see Figure 9 below, which shows very tight standard deviation intervals) that were very consistent between patients and demonstrated higher systemic uptake of GB0139 than in healthy adult males in the Phase 1 part of the trial. This indicates that IPF patients are able to receive an inhaled drug to the peripheral parts of their lungs, which is the site of disease. Although observed at very low plasma concentrations, the higher plasma levels of GB0139 observed in the IPF patients is probably due to a loss of alveolar barrier integrity with increased epithelial permeability, which is present in the fibrotic lung.

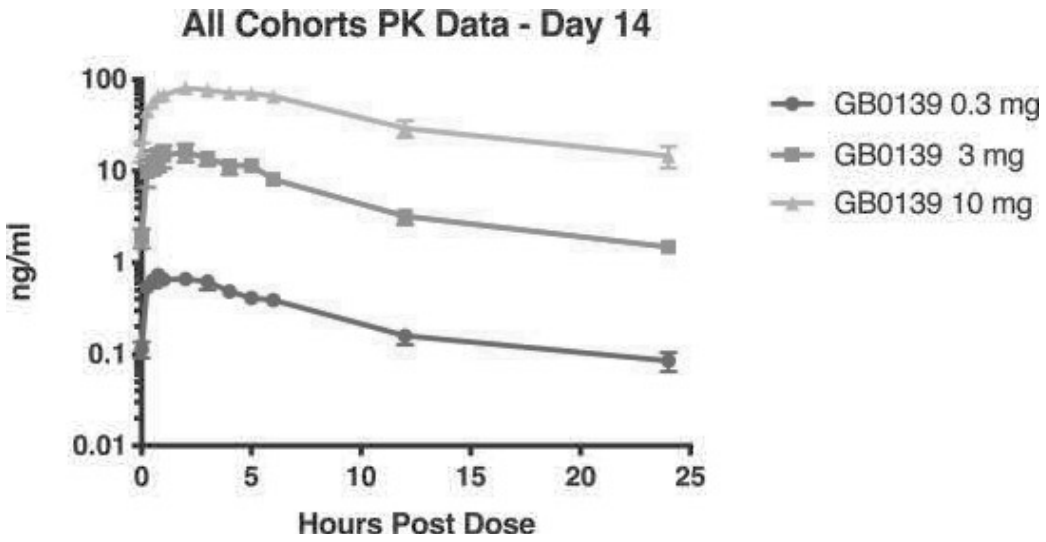


Figure 9. Consistent exposure of GB0139 among IPF patients in Phase 2a trial

We also observed dose-dependent increases in GB0139 levels in alveolar macrophages obtained from the BAL fluid, confirming drug exposure in situ in the lung. There was a significant correlation between plasma levels of GB0139 and levels in the macrophages in BAL fluid (Pearson correlation coefficient 0.89 with $p<0.0001$). However, inhaled dosing of GB0139 resulted in drug levels that were between 567 and 1,930 times higher in alveolar macrophages than in plasma at two hours post-dose on day 14. This large difference in drug levels between plasma and alveolar lung macrophages supports our approach of delivering GB0139 through inhalation to maximize the exposure of the target lung tissue to the drug, while minimizing systemic exposure, which we believe will improve patient safety and tolerability.

Dosing with GB0139 led to dose-dependent decreases in galectin-3 levels on the cell surface of macrophages harvested from the BAL fluid, providing further evidence that GB0139 was able to reach the target tissue and significantly reduce the levels of the galectin-3 target protein attached to macrophages. These cells play an active part in the pathobiology in IPF.

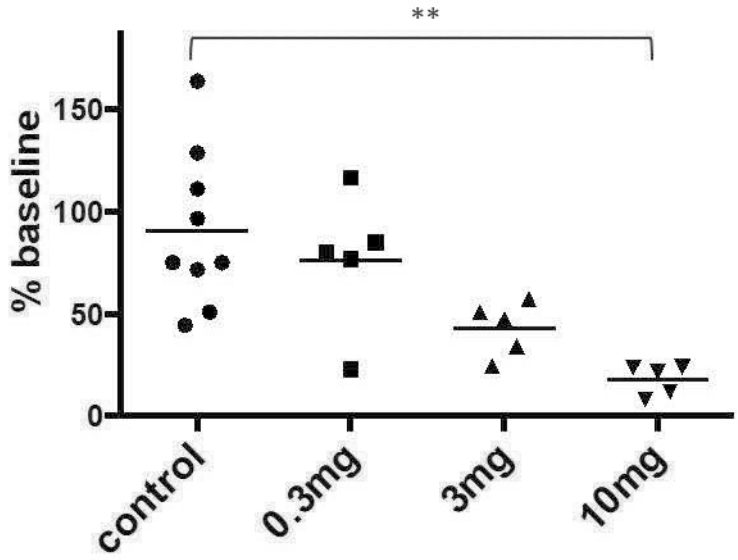


Figure 10. GB0139 led to dose-dependent decrease of galectin-3 in alveolar macrophages

Treatment of IPF patients with GB0139 resulted in decreases in serum levels of a broad panel of biomarkers associated with fibrosis and progression of IPF, as well as decreases in levels of galectin-3. The clear reduction in the serum levels of several fibrosis biomarkers may suggest that treatment with GB0139 had a measurable effect on the parenchymal disease process in the lungs. We believe no other IPF therapeutic has presented data of similar type and magnitude. These include:

- YKL-40, an inflammation-related glycoprotein, the levels of which have been used to predict survival in IPF patients;
- PAI-1, or plasminogen activator inhibitor type -1, a regulator of tissue homeostasis and wound repair that is elevated in fibrosis;
- PDGF-BB, or platelet-derived growth factor, a stimulator of fibroblast growth; and
- CCL-18, or CC Chemokine Ligand 18, a small protein derived from alveolar macrophages that acts as a chemo-attractant and is negatively correlated to pulmonary function tests in IPF patients.

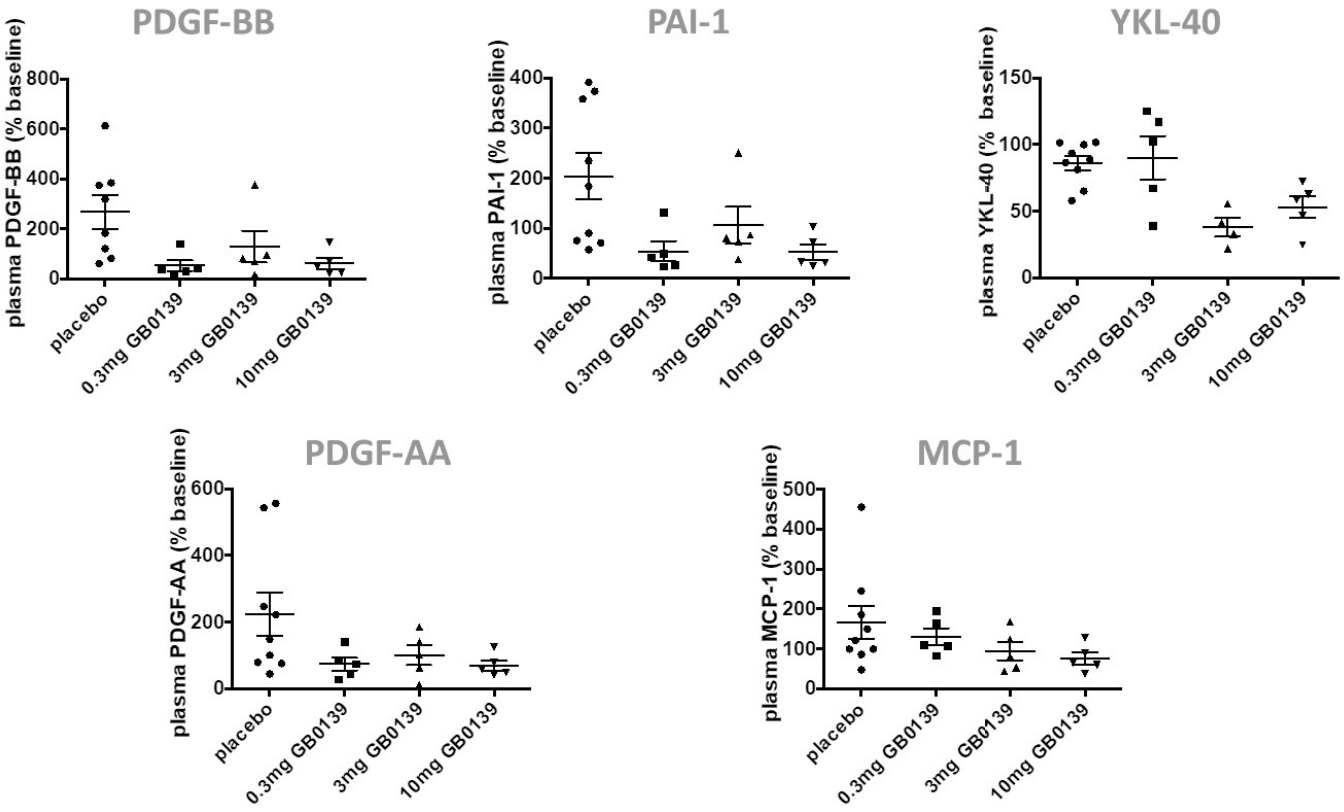


Figure 11. Inhaled GB0139 led to significant reduction in serum levels of a panel of fibrosis biomarkers and correlation between reduction of the plasma biomarkers and the alveolar macrophage surface galectin-3 levels

The observation that these fibrosis-related biomarkers in plasma are concertedly and markedly reduced upon dosing IPF patients with GB0139 supports the key role of galectin-3 in IPF and the potential of GB0139 to generate antifibrotic activity in these patients. The levels of galectin-3 in alveolar macrophages directly correlate with the levels of serum biomarkers of fibrosis, including YKL-40, which has been shown to have prognostic significance in IPF. Four highly relevant disease biomarkers, PDGF, MCP-1, PAI-1 and YKL-40, have been shown to have prognostic significance in IPF and have a well described relationship with myofibroblast activity *in vitro*. In our completed Phase 2a clinical trial, these biomarkers were reduced from baseline in several dose groups compared to placebo and may offer a less invasive measure of pharmacodynamic effects going forward. In a post-hoc analysis of the ASCEND trial and the two CAPACITY trials, which were the three phase 3 clinical trials used for the approval of pirfenidone, YKL-40 was prognostic for progression in the test cohort. However, there was no association between pirfenidone treatment and the longitudinal concentration of any biomarker. In another study comparing treatment naïve IPF patients with those on antifibrotic treatment (pirfenidone or nintedanib), CA-125, CXCL13, MMP7, YKL-40 and OPN predicted differential transplant free survival in treated patients, but at higher thresholds than treatment naïve individuals. There is therefore substantial evidence that several biomarkers are related to disease severity and prognosis, several of which were significantly reduced in plasma of IPF patients after 2 weeks of treatment with inhaled GB0139. The biomarker data suggested a low degree of dose response between the 3mg dose and the 10mg dose. Following the recommendation of the DSMB in March 2021 and the subsequent amendment of the GALACTIC-1 trial protocol, the GALACTIC-1 trial is now evaluating the 3mg dose of GB0139, as compared to placebo, over 52 weeks.

Completed Phase 1/2a Clinical Trial - Phase 1 Part in Healthy Adult Males

In the Phase 1 part of our Phase 1/2a clinical trial conducted in the U.K., we conducted a single ascending dose escalation study in 36 healthy adult males investigating six doses of GB0139 ranging from 0.15mg to 50mg. Inhaled GB0139 was generally well-tolerated in this trial with a half-life of 7 hours, and we observed predictable and well-characterized pharmacokinetics. No drug-related severe adverse events were reported, and other adverse events were mild in severity, and all resolved without intervention.

GB2064 for the Treatment of Myelofibrosis

We are leveraging our knowledge of mechanisms underlying fibrosis and other related diseases to develop product candidates for indications beyond lung fibrosis and targeting pathways that are complementary to galectin-3. We are currently developing GB2064, a selective oral LOXL2 inhibitor, for the treatment of myelofibrosis. The LOXL2 mechanism may also be important in other solid and liquid tumor types as well as fibrotic diseases.

Myelofibrosis Disease Background

Myelofibrosis is one of a number of progressive blood cancers known as myeloproliferative neoplasms and is associated with significantly reduced quality of life and shortened survival. In myelofibrosis, the bone marrow produces fewer blood cells, which leads to multiple negative impacts, including thrombocytopenia, or greater incidence of low platelet counts; anemia, or low red blood cell counts; and an increased need for red-blood-cell transfusions. When bone-marrow based production of blood cells is significantly reduced, myelofibrosis patients also suffer from enlarged spleens due to overabundance of blood-forming stem cells. Myelofibrosis is considered to be a chronic leukemia which, in a subset of patients, can transform into an acute form of leukemia. Median overall survival is approximately 2.25 to 11.25 years. Transformation to acute leukemia is the most common cause of death from myelofibrosis, followed by cardiovascular complications.

Myelofibrosis affects between 16,000 and 18,500 patients in the United States with significant morbidity and mortality. Although the precise cause of myelofibrosis remains unknown, overactive Janus-associated kinase, or JAK, pathway signaling is present in all patients with the disease.

Current Treatments for Myelofibrosis and Their Limitations

The only currently approved specific therapeutic treatments for myelofibrosis are inhibitors of JAK2, consisting of ruxolitinib marketed as JAKAFI® by Incyte in the United States and JAKAVI® by Novartis outside of the United States and fedratinib, marketed as Inrebic® by Celgene/BMS. These kinase inhibitors provide symptomatic benefit, but only modest reductions in bone marrow fibrosis. In patients dosed for four or more years with ruxolitinib, for example, only one-third of patients showed reductions in fibrosis. Additionally, 60% of patients on ruxolitinib become transfusion dependent, versus 38% of patients in the placebo group. 16.8% of patients treated with ruxolitinib and 0.7% of patients treated with placebo developed newly occurring or worsening Grade 1 elevations in cholesterol. The incidence of Grade 2 cholesterol elevations was 0.6% for ruxolitinib with no Grade 3 or 4 cholesterol elevations. Despite this, total worldwide sales of ruxolitinib and fedratinib combined were approximately $3.7 billion and $3.3 billion in 2021 and 2020, respectively.

The only curative treatment for myelofibrosis is an allogeneic hematopoietic stem cell transplant, or HSCT. However, HSCT in myelofibrosis patients is a procedure associated with a high treatment-related mortality rate. Even when HSCT is restricted to the subpopulation of patients who are deemed healthy enough to withstand the treatment, there is a one-year treatment-related mortality rate of between 12 percent and 25 percent. Due to the only modest reductions in fibrosis demonstrated by JAK inhibitors and the high mortality rate associated with HSCT, we believe that significant unmet need remains for new therapeutic options.

Our Solution - GB2064

We have chosen to pursue myelofibrosis as our first indication for GB2064 due to the upregulation of the LOXL2 in a number of fibrotic diseases, including myelofibrosis, the drug activity seen in preclinical data, the rapid rate of progression of the disease, and the relative ease of following disease progression through serum samples and bone marrow biopsies. In preclinical models, GB2064 is approximately 400-fold more selective for human LOXL2 over other human LOX enzymes. GB2064 has shown activity in a number of preclinical models of fibrosis; has demonstrated good pharmacokinetics; and was generally well-tolerated in a Phase 1 trial in healthy adults. While the current standard of care for myelofibrosis consists of inhibitors of the JAK2 protein kinase, which only alleviate the disease symptoms through inhibition of cell proliferation but do not directly target fibrosis, we believe that GB2064 has the potential to be a disease-modifying therapy because it is designed to have a direct impact on the fibrotic process and slow the progression of the disease.

Overview of Ongoing Clinical Trial – MYLOX-1 Trial

During the third quarter of 2021, we initiated the Phase 2a MYLOX-1 trial examining GB2064 for the treatment of myelofibrosis. The primary endpoint of this trial is safety and secondary endpoints include measurements of drug levels in the bone marrow and grade of fibrosis, improvement of anemia and/or thrombocytopenia and assessment of spleen and liver size.

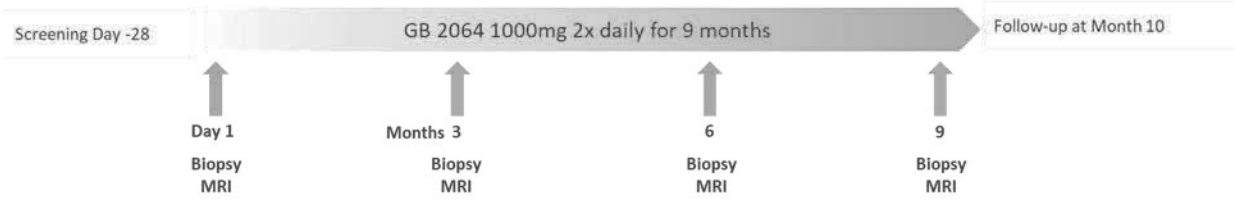


Figure 12. MYLOX-1 trial design

During the third quarter of 2022, we announced data from a planned intermediate assessment. As part of this assessment, we evaluated results from the first five patients who had completed at least six months of treatment with GB2064 and who had repeated bone marrow biopsies. In the intermediate assessment, four out of five evaluable myelofibrosis patients who received GB2064 monotherapy for at least six months experienced a ≥ 1-grade reduction in collagen fibrosis of the bone marrow (see Figure 13 below), an improvement suggesting that GB2064 could impact the progression of the disease and potentially be disease modifying. All four patients who experienced a ≥ 1-grade reduction in fibrosis score also showed stable hematological parameters (hemoglobin, white blood cell count, and thrombocytes) and stable spleen volume over the six month treatment period, and none required transfusion.

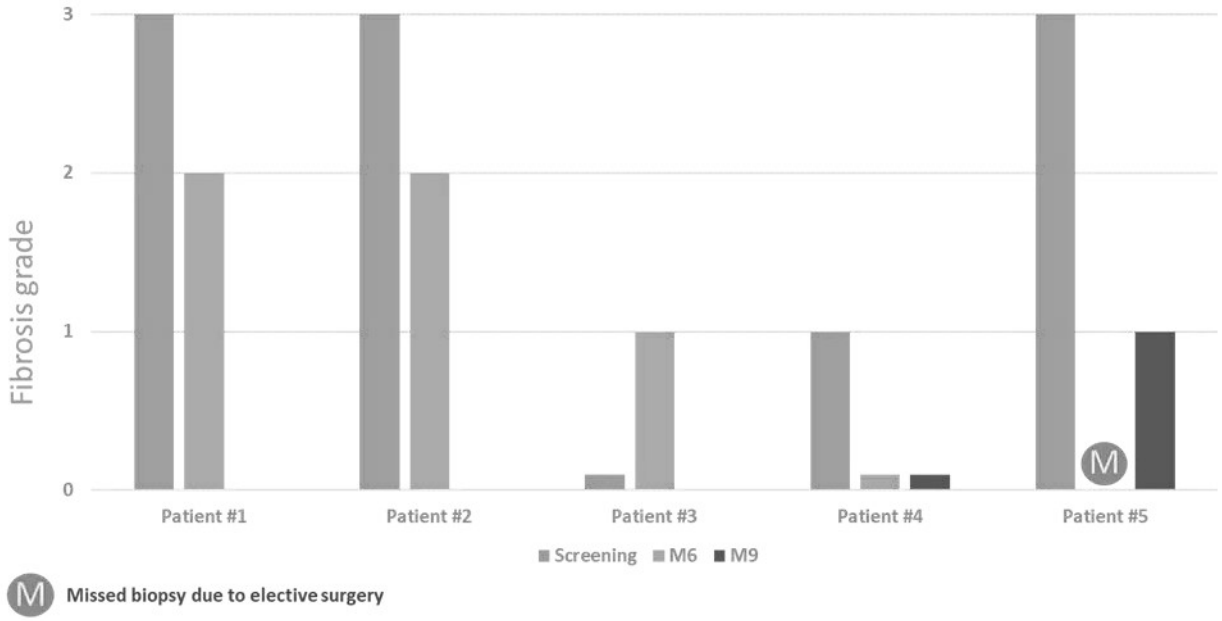


Figure 13. Phase 2a MYLOX-1 trial intermediate assessment - collagen fibrosis grade

As of the date of the planned intermediate assessment, sixteen patients in the MYLOX-1 trial had been dosed with GB2064, of which eight patients had completed or continued to receive treatment and eight patients had either discontinued treatment as a result of an adverse event or disease progression. The most commonly observed treatment-related adverse events were gastrointestinal in nature and were manageable in most patients with standard therapy. In the five patients who completed at least six months of treatment with GB2064, there were no treatment-related serious adverse events, while in the entire trial population, the only possibly treatment-related serious adverse event was a case of fall.

The data from the intermediate assessment of the MYLOX-1 trial suggest that the LOXL2 mechanism may be a way to reduce fibrosis, which we believe has not been shown with any FDA-approved therapy. We continue to enroll patients in the MYLOX-1 trial and expect topline results from the MYLOX-1 trial to be available by the end of 2023. Because the MYLOX-1 trial has already exceeded the pre-defined target of a ≥ 1 grade reduction in collagen fibrosis in at least three patients, we may determine to enroll fewer patients than the sixteen evaluable patients provided for in the protocol. Given that we have already

shown bone marrow collagen reduction and a manageable clinical tolerability profile, we are beginning to plan for next steps in clinical development, which we expect could include combining GB2064 with another myelofibrosis treatment.

Completed Phase 1 Clinical Trial

We have completed a Phase 1 single ascending dose and multiple ascending dose trial of GB2064 in 78 healthy volunteers. Volunteers received single doses of 150, 450, 1000, 2000 or 2500mg of GB2064 or daily doses of 150, 750, 2000mg or placebo for seven days. Dose-dependent increases in serum levels of GB2064 were observed, and using a proprietary assay, we determined that our oral selective inhibitor GB2064 led to dose-dependent inhibition of LOXL2 in serum.

No serious adverse events were reported, and the reported adverse events included nausea, headache, and dizziness that were mild in severity and frequency.

Preclinical Data

In preclinical studies, GB2064 showed activity in multiple models of fibrosis including lung, liver and kidney fibrosis. In a bleomycin-induced model of lung fibrosis, treatment of mice with bleomycin leads to lung fibrosis. Prophylactic dosing of GB2064 led to a significant reduction in fibrosis development in this model. Where fibrosis had already developed, therapeutic dosing of GB2064 led to reductions in further fibrosis development.

LOXL2 is highly expressed in other fibrotic diseases such as renal fibrotic disease. The mouse Col4A3 model of kidney disease is based on a genetic mutation that is found in patients with Alport Syndrome, a rare disease characterized by fibrosis that leads to progressive loss of kidney function among other symptoms such as progressive loss of hearing and retinopathy. LOXL2 expression is significantly elevated in both the kidney cortex and glomeruli in this mouse model. In preclinical studies, treatment of Col4A3 mice with GB2064 has demonstrated an ability to prevent glomerular sclerosis and a scarring of the blood filtering vessels in the kidney and resulted in lower fibrosis scores in the kidney.

GB1211 for the Treatment of Fibrosis and Cancer

We believe GB1211, a selective oral galectin-3 inhibitor, has the potential to treat multiple types of fibrosis and oncology indications. We are developing GB1211 initially for the treatment of liver cirrhosis, a disease with no regulatory approved treatments except for symptomatic therapy or liver transplant and NSCLC, a disease with high mortality and few treatment options. We may also consider developing GB1211 for other cancers and fibrotic diseases and, in October 2022, we expanded our focus on additional oncology indications and entered into an agreement with Providence Portland Medical Center's EACRI to evaluate the safety and efficacy of GB1211 in combination with pembrolizumab for the treatment of metastatic melanoma and HNSCC in an investigator-initiated trial.

Liver Cirrhosis Background

Fibrous tissue accumulation is seen in the liver as a result of continued liver injury driven by a different stimulus or the autoimmune processes. The process of chronic inflammation leads to a progressive accumulation of extracellular matrix, or a scar tissue. Although different chronic liver diseases are characterized by distinct patterns of fibrosis deposition, the development of cirrhosis represents a common outcome and leading to similar clinical consequences, and ultimately liver related death.

Cirrhosis is defined histologically as a diffuse process in which the normal anatomical lobules are gradually replaced by architecturally abnormal nodules separated by fibrous tissue. Different histological scoring systems have been defined to describe the stages of transformation from lack of fibrosis through formation of a portal, periportal and bridging fibrosis to cirrhosis. Our preclinical data suggests that inhibition of galectin-3 may counter established liver cirrhosis and could therefore become one of the first disease-modifying agents for liver cirrhosis.

Current Treatments for Liver Cirrhosis and Their Limitations

There are no FDA approved drugs for liver cirrhosis. In general, therapeutic interventions are limited to supportive care relating to complications caused by the liver not functioning, and, in advanced cases, liver transplantation. As such, this is an area of high unmet medical need.

Galectin-3 in Liver Cirrhosis

Our initial target indication for GB1211 in fibrosis is liver cirrhosis. While the historical view was that established fibrosis is very difficult to impact, our preclinical data suggest that galectin-3 inhibition could reduce established fibrosis and the disease processes that drive the disease progression. Galectin-3 is a central regulator of chronic inflammation and fibrogenesis. Although not present in normal hepatocytes, galectin-3 expression is markedly increased in cirrhotic human liver secondary to a wide range of etiologies including viral-induced liver disease (Hepatitis B and C), NASH, autoimmune, copper or iron overload, primary biliary cirrhosis and alcohol-induced liver disease. Galectin-3 levels are highest in the F3/F4 fibrotic stages compared to F0/F1 and may arise by the impaired hepatic removal and/or by higher hepatic synthesis of galectin-3. Systemic galectin-3 is also increased in alcoholic liver disease and negatively correlates with liver function and Child-Pugh score.

In rodent models, galectin-3 expression is increased temporally in areas of bridging fibrosis and at the periphery of the hepatocyte nodules in the liver following CCl_4 administration. Galectin-3 is also increased in other models of liver fibrosis including thioacetamide-induced and nutritionally deficient, dietary models of hepatocellular and biliary injury in mice. In models of primary biliary cirrhosis, galectin-3 may mediate injury in these models via activation of the inflammasome and IL33/sT2 pathways. Global genetic deletion of galectin-3 results in reduced fibrosis in several models of toxin-induced, dietary- and surgically induced liver fibrosis in mice. These data suggest that galectin-3 up-regulation within the liver is a basic response to liver injury, irrespective of the initiating agent or disease process. As a result, we believe galectin-3 inhibitors have the potential to be a therapy for NASH or liver cirrhosis.

The most advanced clinical studies investigating the blockade of galectin-3 in liver fibrosis have used modified pectins such as belapectin. However, these large complex carbohydrates demonstrate low affinity for the galectin-3 carbohydrate recognition domain (CRD, 11) and with human PK data showing levels of systemic drug at orders of magnitude lower than K_D, this predicts a low chance of any meaningful target engagement in a clinic setting.

We have developed small molecule orally active galectin-3 inhibitors, including GB1211, which demonstrate high (nM) affinity for human galectin-3 and good systemic exposure. GB1211 has been shown to reduce CCl_4-induced liver fibrosis and fibrotic gene expression in mice. In the fourth quarter of 2022, we announced topline results from our Phase 1b/2a GULLIVER-2 trial of GB1211 in patients with decompensated liver cirrhosis that showed statistically significant reductions in liver enzymes after 12 weeks of treatment. We believe that this is the first study in a population of Child-Pugh Class B decompensated cirrhosis patients of non-viral etiology showing changes in a series of liver parameters that are potentially clinically meaningful.

NSCLC Background

Lung cancer is the most common fatal malignancy in the developed world accounting for approximately 1.7 million deaths per year worldwide. In the United States in 2021, it is estimated that there were approximately 236,000 new cases of lung cancer and approximately 132,000 deaths from lung cancer. NSCLC is believed to account for about 85% of all lung cancers.

Current Treatments for NSCLC and Their Limitations

NSCLCs are relatively insensitive to available treatments, which include surgery, irradiation and cytochemical therapy. With the advent of immunotherapy, a new understanding of the interplay between the immune system and cancer has evolved, and it is now increasingly understood that cancer can avoid immune detection and immune killing by a series of mechanisms. The readiness of the immune cells that can detect and kill cancer (including T-cells), the tumor micro-environment, or TME, in which they work, and cancer cell characteristics determine whether or not the immune system will be successful in killing cancer cells. A certain class of immune stimulation therapies have been developed and approved for treating lung cancer. The class is called checkpoint inhibitors, as these are compounds that specifically target and inhibit cell surface molecules, so-called “checkpoints”, that inhibit the activity of the immune system. The most well characterized class, the anti-PD-1 antibodies, have been shown to reduce mortality and increase progression free survival. However, even though these have been introduced in the clinic, mortality from lung cancer remains very high, as only approximately 30% of patients respond to anti-PD-1/PD-L1 therapies and approximately 20% of the patients treated with anti-PD-1/PD-L1 therapy show significant adverse lung effects, including inflammation and fibrosis.

One of the reasons that anti-PD-1/PD-L1 medicines are believed to only show limited efficacy is that factors in the tumor micro-environment reduce T-cell entry and induce T-cell anergy, which leads to reduced T-cell mediated toxicity. We believe one of these TME factors is high levels of galectin-3 in the tumor micro-environment. Galectin-3 has been shown to reduce T-cell entry and activity through binding to cells surface proteins, such as LAG3, PD-1 and the T-cell receptor. Further, galectin-3 disrupts the IFNγ gradient in the tumor, which in turn reduces T-cell chemotaxis. In addition, galectin-3 polarizes the tumor associated macrophage, which also reduce T-cell activation. Hence, blockade of galectin-3 may lead to increased T-cell number and activity in the tumor, though inhibition of these many factors.

Based on the wide tumor and metastasis promoting actions of galectin-3, we believe that our compounds targeting galectin-3 could counter many of the detrimental effects of galectin-3 and may be suitable as single agents or in combination with other checkpoint inhibitors, chemotherapy or chemo-irradiation therapies. Based on the favorable tolerability profile of our compounds observed to date, we believe our galectin-3 inhibitor therapies could be suitable for many clinical situations. In addition to galectin-3 inhibitors, we are progressing galectin-1 and galectin-9 inhibitors which may be useful in certain types of cancer.

Galectin-3 in NSCLC

Galectin-3 inhibition has the potential to both increase T-cell function as a single agent as well as to increase the efficacy of checkpoint inhibitors for NSCLC. In an animal model, we observed that oral administration of our galectin-3 inhibitors reduced human and mouse lung adenocarcinoma growth and blocked metastasis. Treatment with one of our galectin-3 inhibitors also potentiated the effects of a PD-L1 immune checkpoint inhibitor. The mechanisms at work include checkpoint inhibitor-type mechanisms (inhibition of TGF-β signaling, LAG-3, T-cell receptor, interferon gamma) and mechanisms potentially enhancing PD-1/PD-L1 activity, as evidenced by preclinical data that we recently presented at the 2022 American Society of Clinical Oncology Annual Meeting showing that GB1211 reversed a galectin-3 induced blockage of the checkpoint inhibitors atezolizumab and pembrolizumab and exhibited synergistic effects with these checkpoint inhibitors. Furthermore, in the clinic, a retrospective study showed that patients with high tumor staining for galectin-3 were resistant to treatment with pembrolizumab, an anti-PD-1 antibody approved for the treatment of NSCLC, and, by contrast, patients with low galectin-3 had a good response to pembrolizumab and a reduction in tumor volume (see Figure 14 below). Similar data was also seen in melanoma patients, suggesting that the inhibition of galectin-3 may be broadly applicable in a number of cancers and indicating a central role of galectin-3 in the tumor defense mechanisms. Galectin-3 could be a biomarker for anti-PD-1/PD-L1 resistance and, therefore, for patients who may benefit from galectin-3 inhibition. While we will not screen for high galectin-3 in the currently planned GALLANT-1 trial, we do intend to use galectin-3 immunohistochemistry staining in NSCLC to select patients with high galectin-3 levels in the tumor tissue, who may respond to the combination of an anti-PD-1/PD-L1 therapy and our galectin-3 inhibitor GB1211. Because we also measure circulating levels of galectin-3, this may also prove suitable for patient selection. Galectin-3 is an FDA approved biomarker for fibrotic heart disease.

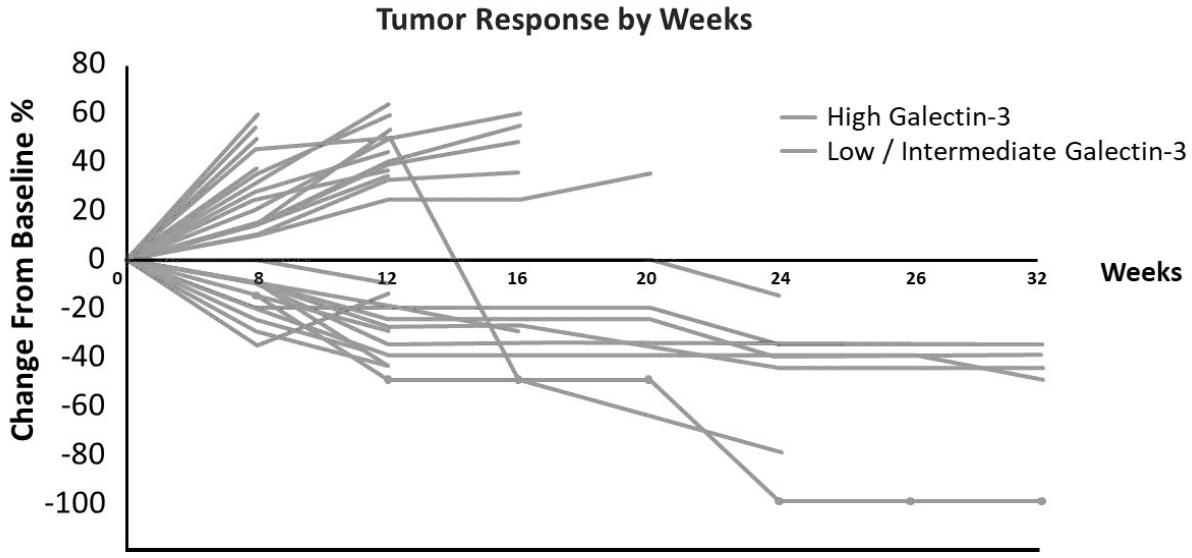


Figure 14. High galectin-3 expression in 34 patients with NSCLC strongly correlated with tumor resistance to pembrolizumab

Our Solution – GB1211

We believe GB1211 has the potential to treat multiple types of fibrosis and oncology indications. We have demonstrated anticancer and fibrosis activity of GB1211 in several preclinical models and have completed a Phase 1 trial in 78 healthy volunteers, where GB1211 showed good pharmacokinetics and was generally well-tolerated. Additionally, GB1211 has shown anticancer effects in preclinical models, specifically in NSCLC tumors high in galectin-3 and resistant to anti-PD-1.

Overview of Clinical Trials

Preclinical Data

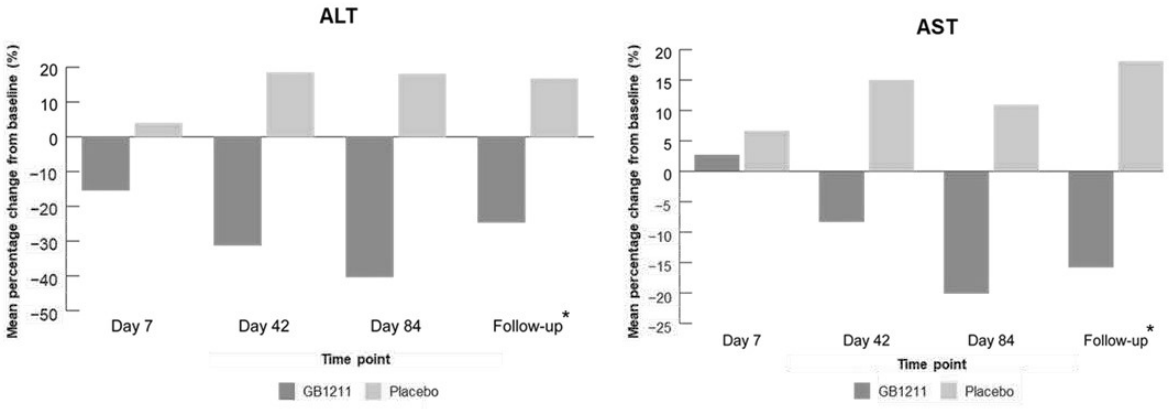
The effect of GB1211 was evaluated in a mouse model of carbon-tetrachloride-induced liver fibrosis. In two separate studies, fibrosis was induced in mice, which were then given either GB1211 or placebo. Mice dosed with 10mg/kg GB1211 twice a day had significantly lower levels of liver fibrosis compared to mice given placebo as detected by histological staining of liver sections with a collagen-specific dye, picrosirius red. This reduction in fibrosis was observed in the absence of changes in liver weight or body weight. These findings were consistent when compared with a standard measurement of collagen content using levels of hydroxyproline, a major component of collagen

Completed Phase 1 Clinical Trial

We have completed a Phase 1 single ascending dose and multiple ascending dose trial of GB1211 in 78 healthy volunteers in the U.K. GB1211 was generally well-tolerated with no drug-related serious adverse events at any doses up to the maximum dose tested of 400mg.

Completed Phase 1b/2a Clinical Trial in Liver Cirrhosis – GULLIVER-2 Trial

During the fourth quarter of 2022, at the American Association for the Study of Liver Diseases' (AASLD) The Liver Meeting® 2022, we announced topline results from our Phase 1b/2a GULLIVER-2 trial of GB1211 that is focused on safety and effect on liver function and fibrosis biomarkers in patients with decompensated liver cirrhosis. These topline results showed statistically significant reductions in ALT ($p<0.0005$), AST ($p<0.005$) and GGT ($p<0.05$), with encouraging reductions for ALP ($p<0.09$), after 12 weeks of treatment. Patients treated with GB1211 also demonstrated improvement and consistent signs of activity across biochemical liver function markers and markers of target engagement, apoptosis, and fibrosis, including reductions in galectin-3 ($p<0.05$) and CK-18 (M65) ($p<0.002$). Bilirubin, albumin, international normalized ratio (INR) and other biochemical measurements remained stable. These findings suggest that GB1211 provided liver cell protection and improved liver status, further supporting clinical development in severe liver disease. Liver enzyme (ALT, AST and GGT) reductions were observed after seven days of treatment and continued to decrease over the 12 weeks of treatment. These liver enzyme levels remained decreased compared to baseline two weeks after the study's conclusion, suggesting durable effects and a decrease in liver inflammation.



Treatment effect (GB1211-Placebo) [%] at Day 84	ALT	AST	GGT	ALP
Mean	-58.44	-32.40	-37.77	-14.76
95% confidence interval	(-79.00, -37.88)	(-51.63, -13.17)	(-69.47 , -6.06)	(-31.92 , -2.40)
p-value	0.0001	0.002	0.0214	0.0889

*Follow up took place two weeks after the last dose. ALT: alanine transferase; AST: aspartate transferase

Figure 15. Topline Phase 1b/2a GULLIVER-2 liver-related biochemistry results

GB1211 exhibited a favorable tolerability profile in patients with decompensated liver cirrhosis in the GULLIVER-2 trial. Five of 15 patients on GB1211 and four of 15 patients on placebo reported nine and eight treatment-emergent adverse events (TEAEs), respectively. Three serious TEAEs consistent with severe liver disease were observed in one patient (2 after cessation of active therapy) on GB1211 and were deemed to be unrelated to GB1211.

The consistency of the reductions in liver enzymes shown in this severe form of liver cirrhosis, the progressive improvement we observed over 12 weeks and the favorable safety profile observed in the GULLIVER-2 trial lead us to believe that a broader study in patients with compensated and/or decompensated cirrhosis could show broader clinical activity, providing a potential regulatory path to approval as the first FDA-approved therapy in liver cirrhosis.

Phase 2a Clinical Trial in NSCLC – GALLANT-1 Trial

In the fourth quarter of 2021, we announced that we had entered into a clinical trial supply agreement with Roche for our Phase 2a GALLANT-1 trial of GB1211 in combination with atezolizumab, a PD-L1 checkpoint inhibitor, for the treatment of first-line NSCLC. This randomized, double blind, placebo-controlled trial is examining the effect of GB1211 and atezolizumab on tumor shrinkage based on RECIST criteria, as well as secondary endpoint measures such as overall survival, progression-free survival and others. We also plan to analyze how plasma galectin-3 levels and tumor galectin-3 correlate with tumor response.

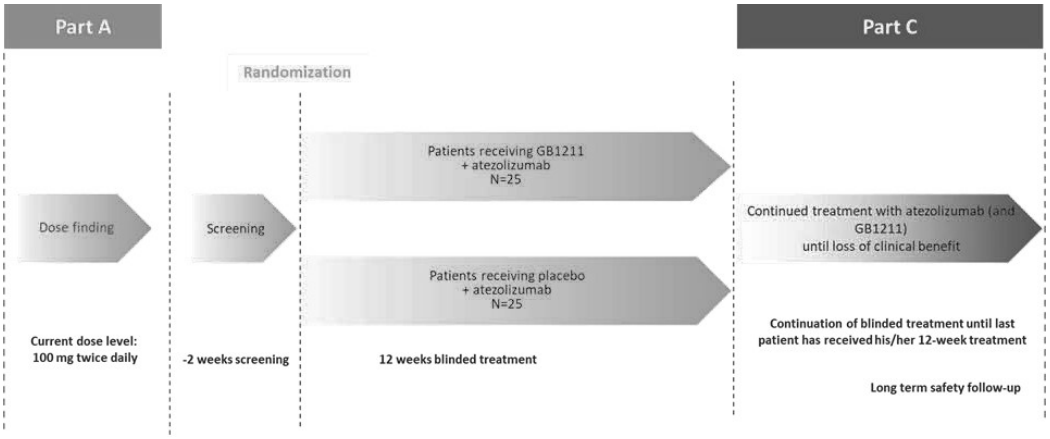


Figure 16. GALLANT-1 trial design

We initiated Part A of this trial, an open-label study to select the dose of GB1211 to be used with atezolizumab, in the second quarter of 2022. In the first 6 patients who received 200mg twice daily in combination with atezolizumab, we observed two serious adverse events of autoimmune-type skin rashes (showing perivascular lymphocytic infiltrates), which were determined by the principal investigator to be related to the administration of atezolizumab. The reactions were similar to those observed with atezolizumab and described in the label. Both reactions responded to therapy with oral glucocorticosteroids and were clinically manageable. In accordance with the protocol, we reduced the GB1211 dose to 100mg twice daily for the second patient cohort. Recruitment in this cohort is currently ongoing. Interestingly, inflammatory and perivascular lymphocytic infiltrates were observed in both skin reactions, and could signal an exaggerated immune activation, something often observed with checkpoint inhibitor therapy and associated with improved clinical outcomes. Because a central aspect of the mechanism of action for GB1211 in combination with a checkpoint inhibitor is to remove galectin-3 from the lymphocytes and the tumor cells, and thereby increase lymphocyte-based tumor killing, we believe this could also be a positive signal of enhanced lymphocyte activation. We expect to release interim safety data from this part of the GALLANT-1 trial in the second quarter of 2023. Part B of this trial is designed to evaluate the safety and tumor shrinkage (based on RECIST criteria) of the combination of the selected dose of GB1211 and atezolizumab and we expect topline results to be available in the first half of 2024.

Phase 2 Investigator-Initiated Trial in Metastatic Melanoma and HNSCC

In October 2022, we expanded our focus on additional oncology indications and entered into an agreement with Providence Portland Medical Center's EACRI to evaluate the safety and efficacy of GB1211 in combination with pembrolizumab in an investigator-initiated trial in metastatic melanoma and HNSCC patients. Galecto has committed to supply GB1211 for this Phase 2 trial. The randomized, double-blind placebo controlled, investigator-initiated Phase 2 trial is expected to evaluate whether the addition of GB1211 increases the response rate of pembrolizumab in metastatic melanoma and HNSCC patients. The study is designed to evaluate GB1211 in combination with the standard therapeutic dose of pembrolizumab in patients with unresectable or metastatic melanoma or recurrent or metastatic HNSCC progressing during or after platinum-containing chemotherapy. In addition to monitoring for toxicity and clinical response, blood and tumor samples will be obtained to assess immunologic measures relevant to galectin-3 biology and checkpoint inhibition. This trial is expected to begin in the second half of 2023 and topline results could be reported as early as 2025.

Competition

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, the expertise of our management team, clinical capabilities, research and development experience and scientific knowledge provide us with competitive advantages, we face increasing competition from many different sources, including biotechnology and biopharmaceutical companies, academic institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are a large number of large biotechnology and biopharmaceutical companies that are currently pursuing the development of products for the treatment of fibrosis and cancer, and smaller number of companies seeking to develop treatments for liver cirrhosis. Companies that we are aware of that are targeting the treatment of fibrotic and related diseases include large companies with significant financial resources such as Pharmaxis Ltd, Biogen, Inc., AbbVie Inc., Gilead Sciences, Inc., Pliant Therapeutics, Inc., Galectin Therapeutics, Inc., FibroGen, Inc., Liminal BioSciences, Inc., Galapagos NV, Bristol Myers Squibb Co., Madrigal Pharmaceuticals, Inc., Inventiva, Akero Therapeutics, Inc., Boehringer Ingelheim, Roche/Genentech and Novartis AG. However, we know of no other companies currently in clinical development with an inhaled or orally available small molecule inhibitor of galectin-3 or an orally available small molecule inhibitor of LOXL2 for myelofibrosis.

Many of our competitors, either alone or with their collaborators, have significantly greater resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing 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. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Additional mergers and acquisitions may result in even more resources being concentrated in our competitors.

Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than products that we may develop. Our competitors also may obtain FDA or regulatory approval from comparable foreign regulatory authorities for their product candidates 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 or make our development more complicated. The key competitive factors affecting the success of our product candidates are likely to be efficacy, safety, cost, and convenience.

Intellectual property

Our owned patents and patent applications relate to our fibrosis-inhibiting compounds and include patents and patent applications directed to new compositions of matter and to methods of treating lung, kidney and liver disorders. As we continue to develop our product candidates, we intend to seek additional patent protection in the United States, EU and in other key commercial markets worldwide.

GB0139

As of March 1, 2023, we owned five patent families that included eight issued U.S. patents, three pending U.S. patent applications, as well as issued and pending foreign counterpart patents and patent applications, relating to our product candidate, GB0139. These patent families include U.S. Patent No. 9,243,021, which is directed to composition of matter of and methods of treatment using compound GB0139; and U.S. Patent Nos. 10,307,403 and 10,369,136, which are directed to composition of matter of and methods of treatment using a polymorphic form of compound GB0139. U.S. Patent No. 9,243,021 is expected to expire in 2033, and U.S. Patent Nos. 10,307,403 and 10,369,136 are expected to expire in 2036, absent any patent term extension. The other issued U.S. patents are expected to expire between 2029 and 2036, absent any patent term extension. If we continue to pursue patent protection, and if any patents issue based on our pending applications, we expect such patents to expire between 2033 and 2040, absent any patent term adjustment and patent term extension in the United States.

GB1211

As of March 1, 2023, we owned three patent families that included three issued U.S. patents, three pending U.S. patent application, as well as pending foreign counterpart patent applications, relating to our product candidate, GB1211. One patent family includes U.S. Patent No. 10,526,360, U.S. Patent No. 10,774,102 and U.S. Patent No. 11,377,464, which are directed to composition of matter of D-galactopyranose compounds of which compound GB1211 is a species. The issued U.S. patents are

expected to expire in 2036, absent any patent term extension. If we continue to pursue patent protection, and if any patents issue based on our pending applications, we expect such patents to expire in 2036, absent any patent term extension in the United States.

Our other patent families include two pending U.S. patent applications and pending foreign counterpart patent applications. If we continue to pursue patent protection, and if any patents issue based on our pending applications, we expect such patents, if issued, to expire in 2040, absent any patent term adjustment and patent term extension in the United States.

GB2064

As of March 1, 2023, we owned three patent families that included five issued U.S. patents, two pending U.S. patent applications, as well as issued and pending foreign counterpart patent and patent applications, relating to our product candidate, GB2064. These patent families include U.S. Patent Nos. 10,150,732, 10,570,094 and 11,072,585, which are directed to composition of matter of and methods of treatment using compound GB2064. These issued U.S. patents are expected to expire in 2036, absent any patent term extension. The third issued patents, U.S. Patent Nos. 10,774,069 and 11,459,309, are directed to crystalline forms of GB2064. These patents are expected to expire in 2037, absent any patent term extension. If we continue to pursue patent protection, and if any patents issue based on our pending applications, we expect such patents to expire between 2036 and 2037, absent any patent term adjustment and patent term extension in the United States.

For a discussion of the risks associated with our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, packaging, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation of Drug Products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The FDA also regulates biological products under the FDCA and the Public Health Service Act, or PHSA. If we advance clinical development of a biologic candidate in the future, these development activities will be subject to additional regulatory requirements specific to biologics. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending New Drug Applications, or NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

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 compliance with the FDA's good laboratory practice, or GLP, regulations;
- Submission to the FDA of an Investigational New Drug application, or IND, which must become effective before human clinical trials may begin;
- Approval of the protocol and related documentation by an independent institutional review board, or 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 practice, or GCP, requirements and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed drug product for each indication;
- Submission to the FDA of an NDA, including payment of application user fees;
- A determination by the FDA within 60 days of its receipt of an NDA to accept the marketing 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 where the product is produced to assess compliance with current Good Manufacturing Practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- Satisfactory completion of FDA audits of clinical trial sites that generated the data in support of the NDA to assure compliance with GCPs and the integrity of the clinical data; and
- FDA review and approval of the NDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as *in vitro* and animal studies to assess potential safety and efficacy. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies.

Prior to commencing an initial clinical trial in humans with a product candidate in the United States, an IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND application. An IND application is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin. Some preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue even after the IND application is submitted. An IND application automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may or may not result in the FDA allowing clinical trials to initiate.

Clinical Trials

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the control of the trial sponsor, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND application. In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it is initiated at that institution, and the IRB must conduct continuing review and reapprove the trial at least annually. The IRB also must review and approve the informed consent form and other clinical trial documentation that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completion.

Certain information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. Failure to timely register a covered clinical study or to submit study results as required can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and both the NIH and FDA signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

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

- Phase 1: The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- Phase 2: The investigational product is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase 3: The investigational product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are 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.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Phase 1, Phase 2 and Phase 3 trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a DSMB or safety review committee. This group provides authorization as to whether or not a trial may move forward at designated check points based on access to certain data from the trial and may recommend halting the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the product candidate as well as 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 product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, 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.

NDA Submission and Marketing Approval

Assuming successful completion of the required clinical testing, the results of preclinical studies and clinical trials, together with detailed information relating to the product candidate's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product candidate for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. The FDA will initially review an NDA for completeness before it accepts it for "filing." Under the FDA's procedures, the agency has 60 days from its receipt of the NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has a goal of ten months from the date of "filing" in which to complete its initial review of a standard NDA for a new molecular entity, and six months from the filing date of a new molecular entity NDA with priority review. Accordingly, this review process typically takes 12 months and eight months, respectively from the date the NDA is submitted to the FDA. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug or a drug that presents difficult questions of safety or efficacy to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which 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.

The FDA also may require the submission of a REMS if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug. A REMS may include one or more elements, including medication guides, physician communication plans, patient package insert and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without a REMS, if required.

Before approving an NDA, the FDA typically will 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 requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter generally describes all of the deficiencies that the FDA has identified in the NDA and contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a product candidate intended to treat a rare disease or condition, which is generally a disease or condition that affects either (i) fewer than 200,000 individuals in the United States, or (ii) more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product candidate with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product is entitled to orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications to market the same product for the same indication for seven years, except in certain limited circumstances. If a product candidate designated as an orphan drug ultimately receives marketing approval for an indication broader than what it was designated for, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan drug has exclusivity. Orphan drug designation entitles sponsors to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Expedited Development and Priority Review Programs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients earlier than under standard FDA development and review procedures.

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for Fast Track status any time before receiving NDA approval, but ideally no later than the pre-NDA meeting. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as priority review, discussed below.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of Breakthrough Therapy designation include the same benefits as Fast Track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. A product may also be eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review and to shorten the FDA's goal for taking action on an NDA for a new molecular entity from ten months to six months from the date of filing.

A product may also be eligible for accelerated approval if it treats a serious or life-threatening disease or condition, generally provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of accelerated approval, the FDA may require that a sponsor perform adequate and well-controlled post-marketing confirmatory trials with due diligence and, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date accelerated approval is granted. Under FDORA, the FDA also has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for products considered for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

Even if a product 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. Fast Track designation, Breakthrough Therapy designation and Priority Review designation do not change the standards for approval but may expedite the development or review process. Drugs granted accelerated approval also must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

U.S. Marketing Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain follow-on applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application, or ANDA, for a generic version of the drug or a 505(b)(2) NDA for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such a follow-on application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of market exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity period covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving follow-on applications that do not reference the protected clinical data. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods or listed patents. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with 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 are continuing, annual user fee requirements for any marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

FDA regulations require that products be manufactured in specific facilities and in accordance with cGMP regulations which require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval of a drug is granted, the FDA may withdraw the 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 mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. 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 holds on post-approval clinical trials;
- Refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or withdrawal of product approvals;
- Product seizure or detention, or refusal to permit the import or export of products; and
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted by a sponsor and any third parties acting on behalf of a sponsor only for the approved indications and in a manner consistent with the approved label for the product. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Other Healthcare Laws

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of drug products for which we obtain marketing approval. Arrangements with third-party payors, healthcare providers and physicians, in connection with the clinical research, sales, marketing and promotion of products, once approved, and related activities, may expose a pharmaceutical manufacturer to broadly applicable fraud and abuse and other healthcare laws and regulations. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below:

- the federal Anti-Kickback Statute, or AKS, which makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, that is intended to induce or reward, referrals including the purchase, recommendation, order or prescription of a particular drug for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. The AKS has been interpreted to apply to arrangements between therapeutic product manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the AKS is violated. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA. On November 20, 2020, the Office of Inspector General, or OIG, finalized further modifications to the federal Anti-Kickback Statute. Under the final rule, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. We continue to evaluate what effect, if any, this rule will have on our business;

- the federal civil and criminal false claims laws, including the FCA, which can be enforced by private citizens through "qui tam" or "whistleblower" actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Pharmaceutical and other healthcare companies have been, and continue to be, prosecuted under these laws, among other things, for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product and for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery. Similar to the AKS, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation;

- HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Like the AKS, the ACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the creation, use, receipt, maintenance or disclosure of individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

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

- the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, or CMS, under the Open Payments Program, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), to certain non-physician providers such as physician assistants and nurse practitioners, and to teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of a pharmaceutical manufacturer's business activities could be subject to challenge under one or more of such laws. Efforts to ensure that business arrangements comply with applicable healthcare laws involve substantial costs. It is possible that governmental and enforcement authorities will conclude that a pharmaceutical manufacturer's business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against a pharmaceutical manufacturer, and it is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, imprisonment, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, reporting obligations and oversight if we become subject to integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the results of operations. In addition, commercialization of any drug product outside the United States will also likely be subject to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state and federal health information privacy laws, and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of health-related and other personal information. For example, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect into effect on January 1, 2020, and the California State Attorney General has submitted various versions of final regulations. Since July 1, 2020, the California State Attorney General has had the authority to commence enforcement actions against violators. Further, a California privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020 and entered into force on January 1, 2023. The CPRA creates additional obligations with respect to processing and storing personal information. We will continue to monitor developments related to the CPRA and anticipate additional costs and expenses associated with CPRA compliance. Other U.S. states also are considering omnibus privacy legislation (with one additional law already passed in Colorado, Connecticut, Utah and Virginia) and industry organizations regularly adopt and advocate for new standards in these areas. While the CCPA, as modified by the CPRA contain an exception for certain activities involving PHI under HIPAA, we cannot yet determine the impact the CCPA, CPRA or other such future laws, regulations and standards may have on our business, as these laws either do not yet apply to us or are not yet in effect.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions, under state and federal law or other obligations. We may become or are already subject to data privacy laws in other countries, including the EU General Data Protection Regulation, or EU GDPR, in Europe.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Economic Area, or EEA, including personal health data, is subject to the GDPR and similar processing of personal data regarding individuals in the U.K. is subject to the U.K. General Data Protection Regulation, or U.K. GDPR, and the U.K. Data Protection Act 2018. In this Annual Report on Form 10-K, GDPR refers to both the EU GDPR and the U.K. GDPR, unless specified otherwise. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA/U.K., including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million (£17.5 million) or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure compliance.

Current and Future Healthcare Reform Legislation

In both the United States and certain foreign jurisdictions, there have been, and continue to be, a number of legislative and regulatory changes to the health care system. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In particular, in 2010, the ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research.

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Other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- The U.S. Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. Subsequent legislation extended the 2% reduction which remains in effect through 2030. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation.
- The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.
- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded

access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.
- On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.

The Inflation Reduction Act of 2022, or the IRA, includes provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries to $2,000, impose new manufacturer financial liability on certain drugs covered under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The effects of the IRA on our business and the healthcare industry in general is not yet known.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

There have been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. On December 27, 2018, the District Court for the District of Columbia invalidated a reimbursement formula change under the 340B drug pricing program, and CMS subsequently altered the FYs 2019 and 2018 reimbursement formula on specified covered outpatient drugs ("SCODs"). The court ruled this change was not an "adjustment" which was within the Secretary's discretion to make but was instead a fundamental change in the reimbursement calculation. However, most recently, on July 31, 2020, the U.S. Court of Appeals for the District of Columbia Circuit overturned the district court's decision and found that the changes were within the Secretary's authority. On September 14, 2020, the plaintiffs-appellees filed a Petition for Rehearing En Banc (i.e., before the full court), but was denied on October 16, 2020. Plaintiffs-appellees filed a petition for a writ of certiorari at the Supreme Court on February 10, 2021 and the petition was granted on July 2, 2021. On June 15, 2022, the Supreme Court unanimously reversed the Court of Appeals' decision, holding that HHS's 2018 and 2019 reimbursement rates for 340B hospitals were contrary to the statute and unlawful. We continue to review developments impacting the 340B program.

In addition, individual states in the United States have also increasingly passed legislation and implemented 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.

Legislative and regulatory proposals and enactment of laws, at the foreign federal and state levels, directed at containing or lowering the cost of healthcare, will continue into the future. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Regulation Outside the United States

In addition to regulations in the United States, we 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. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Although many of the issues discussed above with respect to the United States apply similarly in the context of the EU and in other jurisdictions, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Whether or not we 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. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials. In the EU, for example, a clinical trial authorization application, or CTA, must be submitted for each clinical protocol to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country's requirements, the clinical trial may proceed.

The requirements and processes governing the conduct of clinical trials vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP, the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational medicinal product under EU regulatory systems, we must submit a marketing authorization application. The content of the NDA filed in the United States is similar to that required in the EU, with the exception of, among other things, country-specific document requirements.

For other countries outside of the EU and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product development, the conduct of clinical trials, manufacturing, distribution, marketing approval, product licensing, pricing and reimbursement vary from country to country.

Countries that are part of the EU, as well as countries outside of the EU, have their own governing bodies, requirements, and processes with respect to the approval of drug products. 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.

Additionally, to the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

Authorization Procedures in the EU

In the EEA (comprised of the EU Member States plus Iceland, Liechtenstein and Norway), medicinal products must be authorized for marketing by using either the centralized authorization procedure or one of the national authorization procedures.

- *Centralized procedure*—If pursuing marketing authorization of a product candidate for a therapeutic indication under the centralized procedure, following the opining of the EMA's Committee for Medicinal Products for Human Use, or CHMP, the EC issues a single marketing authorization valid across the EEA. The centralized procedure is compulsory for human medicines derived from biotechnology processes or advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), products that contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases, and officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the medicine concerned contains a new active substance not yet authorized in the EEA, or is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the EEA. Under the centralized procedure, the maximum timeframe for the evaluation of a marketing authorization application, or MAA, by the EMA is 210 days, excluding "clock stops", when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP, and which can add materially to the timeframe. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

- Now that the U.K. (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Irish Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the U.K. medicines regulator, may rely on a decision taken by the EC on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required.

- *National authorization procedures*—There are also two other possible routes to authorize products for therapeutic indications in several countries, which are available for products that fall outside the scope of the centralized procedure:

- *Decentralized procedure*—Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EEA country of medicinal products that have not yet been authorized in any EEA country and that do not fall within the mandatory scope of the centralized procedure.

- *Mutual recognition procedure*—In the mutual recognition procedure, a medicine is first authorized in one EEA member state, in accordance with the national procedures of that country. Following this, additional marketing authorizations can be sought from other EEA countries in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

In the EU, new products for therapeutic indications that are authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization 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 ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization 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.

The criteria for designating an "orphan medicinal product" in the EEA are similar in principle to those in the United States. In the EEA, 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. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year orphan market exclusivity period, no marketing authorization application shall be accepted, and no marketing authorization shall be granted for a "similar medicinal product" for the same indication. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. The ten-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, marketing authorization may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder of the authorized orphan product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder of the authorized orphan product cannot supply enough orphan medicinal product.

As in the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

In April 2014, the EU adopted the new Clinical Trials Regulation (EU) No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022. The transitory provisions of the new Regulation provide that, by January 31, 2025, all ongoing clinical trials must have transitioned to the new Regulation. The new Regulation overhauls the system of approvals for clinical trials in the EU. Specifically, it is directly applicable in all Member States (meaning that no national implementing legislation in each Member State is required), and aims at simplifying and streamlining the approval of clinical trials in the EU. The main characteristics of the new Regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all Member States of the European Union, or EU Member States, in which an application for authorization of a clinical trial has been submitted (Concerned Member States) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications.

Should we utilize third-party distributors, compliance with such foreign governmental regulations would generally be the responsibility of such distributors, who may be independent contractors over whom we have limited control.

Brexit and the Regulatory Framework in the U.K.

The U.K. formally left the EU (commonly referred to as "Brexit") on January 31, 2020, and the EU and the U.K. have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not provide for wholesale mutual recognition of U.K. and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework continues to apply in Northern Ireland). Except in respect of the new EU Clinical Trials Regulation, the regulatory regime in Great Britain therefore largely aligns with EU regulations, however it is possible that these regimes will diverge more significantly in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and E.U. pharmaceutical legislation.

Coverage and Reimbursement

Successful commercialization of new drug products depends in part on the extent to which reimbursement for those drug products will be available from government health administration authorities, private health insurers, and other organizations. In the United States, government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drug products they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford a drug product. Sales of drug products depend substantially, both domestically and abroad, on the extent to which the costs of drugs products are paid for by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drug products. Third-party payors are increasingly challenging the price, examining the medical necessity, and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. 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. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on its investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for drug products but monitor and control company profits. Accordingly, in markets outside the United States, the reimbursement for drug products may be reduced compared with the United States.

In the United States, the principal decisions about reimbursement for new drug products are typically made by CMS, an agency within the HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a drug product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;

- cost-effective; and
- neither experimental nor investigational.

We cannot be sure that coverage or reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Reimbursement may impact the demand for, or the price of, any product for which we obtain regulatory approval.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the Medicare Modernization Act, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each Part D prescription drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the average manufacturer price, or AMP, and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As the required 340B discount is determined based on average manufacturer price, or AMP, and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by HHS, the Agency for Healthcare Research and Quality and the NIH, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidates, if any such drug or the condition that they are intended to treat are the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our product candidate. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

These laws and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Outside of the United States, the pricing of pharmaceutical products and medical devices is subject to governmental control in many countries. For example, in the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. Other countries may allow companies to fix their own prices for products but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products and medical devices will likely continue as countries attempt to manage healthcare expenditures.

Human Capital

As of December 31, 2022, we had 45 full-time employees, including six who hold M.D. degrees and 14 who hold Ph.D. degrees. Most of our employees work from our offices in Denmark, Sweden, the U.K. and the United States. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be strong.

With our science and knowledge at the center of our business, we have a team of knowledgeable and highly skilled employees who are crucial to the success of our business. As we strive to be an employer of choice and maintain the strength of our workforce, we consistently assess the current business environment and labor market to refine our compensation and benefits programs and other resources available to our employees. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives. We believe that a compensation program with both short-term and long-term awards provides fair and competitive compensation and aligns employee and stockholder interests, including incentivizing business performance and integrating compensation with our overall business plans and strategy.

We are committed to investing in the development of our people and creating an environment where diverse perspectives and backgrounds are encouraged and supported. We host weekly company-wide sessions where ideas are discussed, feedback on corporate initiatives is received, scientific breakthroughs are shared, and other corporate updates are provided. Our people's voices are central to identifying how we, as an organization, can strengthen the organization further and maintain high retention. In 2022, we initiated a bi-annual employee satisfaction survey throughout the organization, showing strong engagement scores throughout 2022. Our future focus is to maintain and grow employee satisfaction by working systematically based on the feedback received from our team.

Diversity, equality, and inclusion are fundamental pillars of our culture, and have been since Galecto was founded in 2011. We believe that an equitable and inclusive environment with diverse teams creates higher engagement, better solutions, and higher productivity, and is crucial to our efforts to attract and retain key employees and improve the business. The composition of our organization accounts for more than 15 different nationalities and our workforce is 53% male and 47% female. Among our leadership team, 62.5% are male and 37.5% are female.

Available Information

Our Internet address is www.galecto.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy, and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or SEC. Information on our website is not part of this Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, including our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K and in the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred significant net losses since our inception and have financed our operations principally through equity and debt financing. We continue to incur significant research and development and other expenses related to our ongoing operations. For the years ended December 31, 2022 and 2021, we reported a net loss of $61.6 million and $51.8 million, respectively. As of December 31, 2022, we had an accumulated deficit of $217.7 million. We have devoted substantially all of our resources and efforts to research and development, and we expect that it will be several years, if ever, before we generate revenue from product sales. Even if we receive marketing approval for and commercialize one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to develop and market additional potential product candidates.

We expect to continue to incur significant losses for the foreseeable future, and we anticipate that our expenses will increase substantially if, and as, we:

- advance our most advanced product candidate, GB0139, our other current fibrosis and oncology product candidates and any future product candidates through clinical development, and, if successful, later-stage clinical trials;
- advance our preclinical development programs into clinical development;
- experience delays or interruptions to preclinical studies, clinical trials, our receipt of services from our third-party service providers on whom we rely, or our supply chain, including delays and economic uncertainty in various global markets caused by geopolitical instability and conflict and economic challenges caused by the COVID-19 pandemic;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- commercialize GB0139, our other current fibrosis and oncology product candidates and any future product candidates, if approved;
- increase the amount of research and development activities to discover and develop product candidates;
- hire additional clinical development, quality control, scientific and management personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development and manufacturing efforts, general and administrative functions and our operations as a public company;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any products for which we may obtain marketing approval and intend to commercialize on our own or jointly with third parties;
- maintain, expand and protect our intellectual property portfolio; and
- invest in or in-license other technologies or product candidates.

To become and remain profitable, we must develop and eventually commercialize products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials, obtaining marketing approval for product candidates, manufacturing, marketing and selling products 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 revenue that is significant enough to achieve profitability. 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.

We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs, future commercialization efforts or other operations.

Developing biotechnology and biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our planned and ongoing clinical trials of GB0139, GB2064 and GB1211 and any future product candidates that we may develop, seek regulatory approvals for any of our product candidates and to launch and commercialize any products for which we receive regulatory approval. We also expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to maintain our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce or eliminate one or more of our research and drug development programs or future commercialization efforts.

As of December 31, 2022, we had $66.1 million in cash, cash equivalents and marketable securities. Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. Our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect, and in any event, we will require additional capital in order to complete clinical development of any of our current programs. Changes in economic conditions, including rising inflation and interest rates, lower consumer confidence, volatile equity capital markets and lower market prices for our securities, ongoing supply chain disruptions and geopolitical instability may adversely affect our business, our future capital requirements and our ability to finance our future cash needs. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development, marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our product candidates, including GB0139, GB2064, GB1211 and any our other product candidates we develop in the future;
- the clinical development plans we establish for these product candidates;
- the number of, and development requirements for, other product candidates that we develop;
- the timelines of our clinical trials and the overall costs to finish the clinical trials due to geopolitical instability and conflict and economic challenges caused by the COVID-19 pandemic;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the European Medicines Agency, or EMA, and other comparable foreign regulatory authorities;
- our ability to enter into contract manufacturing arrangements for supply of active pharmaceutical ingredient, or API, and manufacture of our product candidates, and the terms of such arrangements;
- whether we are able to enter into and maintain collaboration agreements, including the terms of and timing of payments under any such agreements;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;

- the extent to which we acquire or in-license other products, product candidates, or technologies;
- the effect of competing clinical, technological and market developments;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities;
- changes in economic conditions, including rising inflation and interest rates, lower consumer confidence and volatile equity capital markets; and
- the costs of continuing to operate as a public company.

We do not have any committed external source of funds or other support for our development efforts, and we cannot be certain that additional funding will be available on acceptable terms, if at all. Until we can generate sufficient revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. Volatility in equity capital markets may adversely affect the market price of our equity securities, which may materially and adversely affect our ability to fund our business through public or private sales of equity securities. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, our existing stockholders could suffer significant dilution, and any new equity securities we issue could have rights, preferences, and privileges superior to those of holders of our common stock. In addition, any debt financing may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable intellectual property or other rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also may be required to seek collaborators for any of our product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. Market volatility and economic uncertainty in various global markets resulting from geopolitical instability and conflict and economic challenges caused by the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

The amount of our future losses is uncertain and our operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to successfully recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts;
- our ability to obtain marketing approval for our product candidates, and the timing and scope of any such approvals we may receive;
- the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- our ability to attract, hire and retain qualified personnel;

- expenditures that we will or may incur to develop additional product candidates;
- the level of demand for our product candidates should they receive approval, which may vary significantly;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future therapeutics that compete with our product candidates;
- general market conditions or extraordinary external events, such as increased economic uncertainty in the United States and abroad or the economic challenges caused by the COVID-19 pandemic;
- the changing and volatile U.S. and global economic environments; and
- future accounting pronouncements or changes in our accounting policies.

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

Risks Related to Research and Development and the Biotechnology and Biopharmaceutical Industry

We have a limited operating history, which may make it difficult to evaluate our prospects and likelihood of success.

We are a clinical-stage biotechnology company with a limited operating history. We were founded as Galecto Biotech AB, a Swedish operating company, in 2011 and incorporated in Delaware as Galecto, Inc. in October 2019, have no products approved for commercial sale and have not generated any revenue. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of our product candidates. Our approach to the discovery and development of product candidates is unproven, and we do not know whether we will be able to develop any products of commercial value. In addition, our product candidates, including GB0139, for the treatment of IPF, GB1211 for the treatment of various oncology indications and liver cirrhosis, and GB2064 for the treatment of myelofibrosis, are in the early stages of clinical development. These three programs will require substantial additional development and clinical research time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We have not yet demonstrated the ability to progress any product candidate through later-stage clinical trials leading to successful marketing authorization. We may be unable to obtain regulatory approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, achieve market access, and acceptance with insurers and health care providers, or conduct sales and marketing activities necessary for successful product commercialization. Investment in biotechnology and biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by early-stage biotechnology and biopharmaceutical companies in rapidly evolving fields. Consequently, we have no meaningful history of operations upon which to evaluate our business, and 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 drug products.

Our business is highly dependent on the success of our product candidates, GB0139, GB1211, GB2064, as well as any other product candidates that we advance into the clinic. All of our product candidates may require significant additional preclinical and clinical development before we may be able to seek regulatory approval for and launch a product commercially.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We are very early in our development efforts, and our product candidates, including GB0139, are in early clinical development. Because GB0139 is our most advanced product candidate, if GB0139 encounters safety or efficacy problems, development delays, regulatory issues or other problems, our development plans and business would be significantly harmed. We have completed a placebo-controlled Phase 2a multi-dose trial of GB0139 in 24 IPF patients. We are currently conducting a Phase 2b placebo-controlled clinical trial of GB0139 in IPF patients and we expect to release topline results in mid-2023. The primary endpoint of the trial is to assess annual rate of decline in forced vital capacity, or FVC, after one year of dosing. Reduction in decline of FVC is the primary endpoint that was accepted by the FDA for the approval of both of the currently approved treatments

for IPF. For future clinical trials of GB0139, including a Phase 3 clinical trial or trials, the design, duration, and scope of such clinical trials will be decided upon after further discussions with FDA or the EMA, as applicable. As a result, we are unable to predict with certainty the estimated timing or scope of future clinical trials of GB0139 we may conduct.

Before we can generate any revenue from sales of our most advanced product candidate, GB0139, or any of our other fibrosis or oncology product candidates, we must undergo additional preclinical and clinical development, regulatory review and approval in one or more jurisdictions. In addition, if one or more of our product candidates are approved, we must ensure access to sufficient commercial manufacturing capacity and conduct significant marketing efforts in connection with any commercial launch. These efforts will require substantial investment, and we may not have the financial resources to continue development of our product candidates.

We may experience setbacks that could delay or prevent regulatory approval of, or our ability to commercialize, our product candidates, including:

- negative or inconclusive results from our preclinical studies or clinical trials or positive results from the clinical trials of others for product candidates similar to ours leading to their approval, and evolving to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- product-related side effects experienced by patients or subjects in our clinical trials or by individuals using drugs or therapeutics that we, DSMBs, institutional review board, or IRBs, the FDA, other regulators or others view as relevant to the development of our product candidates;
- delays in submitting INDs or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials, including our clinical endpoints;
- delays in enrolling subjects in clinical trials, including due to geopolitical instability and conflict in Eastern Europe and the economic challenges caused by the COVID-19 pandemic;
- high drop-out rates of subjects from clinical trials;
- inadequate supply or quality of product candidates or other materials necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- inability to compete with other therapies;
- poor efficacy of our product candidates during clinical trials;
- trial results taking longer than anticipated;
- trials being subjected to fraud or data capture failure or other technical mishaps leading to the invalidation of our trials in whole or in part;
- the results of our trials not supporting application for conditional approval in the EU;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical development generally or with respect to our technology in particular; or
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and our manufacturing, marketing, distribution and sales efforts or that of any future collaborator.

Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome, and the results of preclinical studies and early-stage clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials.

To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. In particular, the general approach for FDA approval of a new drug is dispositive data from two well-controlled, Phase 3 clinical trials of the relevant drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. A product candidate can fail at any stage of testing, even after observing promising signals of activity in earlier preclinical studies or clinical trials. 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. For example, in our earlier clinical trials, we did not identify any imbalance in the serious adverse events across study groups, in contrast to what was reported to us in March 2021 by the DSMB in our ongoing Phase 2b trial of GB0139. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biotechnology and biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved as therapeutic products, and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of GB0139 or any of our other fibrosis or oncology product candidates. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- preclinical studies or clinical trials may show the product candidates to be less effective than expected (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful;
- failure to receive the necessary regulatory approvals;
- manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that make a product candidate uneconomical; and
- the proprietary rights of others and their competing products and technologies that may prevent one of our product candidates from being commercialized.

In addition, differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products.

Additionally, several of our past, planned and ongoing clinical trials utilize an “open-label” trial design, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may also be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

In addition, the standards that the FDA and comparable foreign regulatory authorities use when regulating our product candidates require judgment and can change, which makes it difficult to predict with certainty how they will be applied. Although we are initially focusing our efforts on development of small molecule drug products, we may in the future pursue development of biological products, which could make us subject to additional regulatory requirements. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations. Examples of such regulations include future legislation or administrative action, or changes in FDA policy during the period of product development and FDA regulatory review. We cannot predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. The FDA may also require a panel of experts, referred to as an advisory committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the advisory committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop.

We are currently conducting clinical trials in foreign countries, as well as in the United States. If we continue to seek to conduct clinical trials in foreign countries or pursue marketing approvals in foreign jurisdictions, we must comply with numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval from foreign regulatory agencies may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the United States and vice versa.

Successful completion of clinical trials is a prerequisite to submitting a marketing application to the FDA and similar marketing applications to comparable foreign regulatory authorities, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We may experience negative or inconclusive results, which may result in our deciding, or our being required by regulators, to conduct additional clinical studies or trials or abandon some or all of our product development programs, which could have a material adverse effect on our business.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of GB0139 or any of our other fibrosis or oncology product candidates in development.

We may experience delays in initiating or completing clinical trials. We also may experience numerous unforeseen events during, or as a result of, any future clinical trials that could delay or prevent our ability to receive marketing approval for, or to commercialize, GB0139 or any of our other fibrosis or oncology product candidates in development, including:

- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the FDA or other comparable regulatory authorities may disagree with our clinical trial design, including with respect to dosing levels administered in our planned and ongoing clinical trials, which may delay or prevent us from initiating or continuing our clinical trials with our originally intended trial design;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- due to the impact of economic challenges caused by the COVID-19 pandemic and uncertainty in various global markets caused by geopolitical instability, we may experience delays or interruptions to our manufacturing supply chain, or we could suffer delays in reaching, or we may fail to reach, agreement on acceptable terms with third-party service providers on whom we rely;

- additional delays and interruptions to our clinical trials could extend the duration of the trials and increase the overall costs to finish the trials as our fixed costs are not substantially reduced during delays;

- we may elect to, or regulators, IRBs, DSMBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- we may not have the financial resources available to complete our planned and ongoing clinical trials, or the cost of clinical trials of any product candidates may be greater than we anticipate;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate to initiate or complete a given clinical trial; and

- the FDA or other comparable foreign regulatory authorities may require us to submit additional data such as long-term toxicology studies or impose other requirements before permitting us to initiate a clinical trial.

Our product development costs will increase if we experience additional delays in clinical testing or in obtaining marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. In addition, we may voluntarily redesign or otherwise modify our plans with respect to an ongoing or planned clinical trial, and changing the design of a clinical trial can be expensive and time consuming. If we do not achieve our product development goals in the time frames we announce and expect, the approval and commercialization of our product candidates may be delayed or prevented entirely. Significant clinical trial modifications or delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any changes or delays in our clinical development programs may harm our business, financial condition and results of operations significantly.

Our ongoing and future clinical trials may reveal significant adverse events or unexpected drug-drug interactions not seen in our preclinical studies and may result in a safety profile that could delay or prevent regulatory approval or market acceptance of any of our product candidates.

We have completed a placebo-controlled Phase 2a multi-dose trial of GB0139 in 24 IPF patients and, with the exception of a number of minor reported adverse events (fever, upper respiratory tract infection, abnormal taste in mouth, dry throat), GB0139 was observed to be generally well-tolerated in these patients with no serious drug-related adverse events. We are currently conducting a double-blind placebo-controlled Phase 2b trial of GB0139. In March 2021, the DSMB for this trial recommended that, based upon a safety analysis of the data, the company discontinue dosing and enrolling patients in the 10mg arm along with patients in the 3mg arm who are receiving combination treatment with the currently approved treatments of IPF, nintedanib and pirfenidone. The DSMB informed the company, based on unblinded safety and efficacy data, that there was an imbalance in the serious adverse events across the study groups, but not an imbalance between the groups in mortality.

Our product candidates are designed to inhibit galectin-3 or LOXL2, and we believe such inhibition can play a key role in regulating fibrosis and cancer. However, our products are still in the testing phase. If significant adverse events or other side effects are observed in any of our ongoing or future clinical trials, including of GB0139 for the treatment of IPF, GB02064 for the treatment of myelofibrosis or GB1211 for the treatment of liver cirrhosis and NSCLC, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials, or we may be required to reduce the dosage amount of our intended product candidate or abandon the trials or our development efforts altogether. For instance, in the dose selection phase of our Phase 2a GALLANT-1 trial for the first-line treatment of NSCLC, we observed two serious adverse events of autoimmune-type skin rashes (showing perivascular lymphocytic infiltrates), which were determined by the principal investigator to be related to the administration of atezolizumab. The reactions were similar to those observed with atezolizumab and described in the label, however, in accordance with the protocol, we reduced the GB1211 dose to 100mg twice daily for the second patient cohort. Some potential therapeutics developed in the biotechnology and biopharmaceutical industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies.

If we continue to encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of completion of our clinical studies depends in part on the speed at which we can recruit patients to participate in

testing our product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States.

From 2020 to 2022, the COVID-19 pandemic caused delays in certain of our studies, including (i) a delay in recruitment for our ongoing Phase 2b trial of GB0139 in IPF patients, which has resulted in certain trial protocol amendments and increased costs and (ii) a delay in the initiation and recruitment of our planned and ongoing clinical trials of GB1211 and GB2064. We may continue to experience difficulties in patient enrollment in our clinical trials for a variety of reasons. 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 trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility and exclusion criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints and the process for identifying patients;
- the willingness or availability of patients to participate in our trials (including due to fears of contracting COVID-19 and other highly infectious or contagious diseases) or known or perceived risks associated with our product candidates;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- the availability of competing commercially available therapies and other competing product candidates' clinical trials;
- our ability to obtain and maintain patient informed consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

For example, we are initially developing GB0139 for the treatment of IPF, which is an orphan indication. In the United States, IPF is estimated to affect approximately 100,000 patients in the United States alone. As a result, we may encounter difficulties enrolling subjects in our clinical trials of GB0139 due, in part, to the small size of this patient population. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Certain of our clinical trials may also involve invasive procedures, such as bone marrow biopsies in our MYLOX-1 trial, which may lead some patients to drop out of trials to avoid these follow-up procedures.

Further, timely enrollment in clinical trials is reliant on clinical trial sites which may be adversely affected by global health matters, including, among other things, pandemics and political and social conditions. For example, the COVID-19 pandemic and military action and civil and political unrest in regions where we have operations have affected certain of our clinical trial sites as they have not been allowed to enroll or recruit patients and other sites have not been able to receive patient visits, which resulted in the need to amend our protocol for our GALACTIC-1 trial in IPF. In addition, after enrollment in these trials, if patients contract COVID-19 during participation in our trials or are subject to isolation or shelter-in-place restrictions, they may drop out of our trials, miss scheduled doses or follow-up visits, or otherwise fail to follow trial protocols. If patients are unable to follow the trial protocols or if our trial results are otherwise disputed due to the effects of the COVID-19 pandemic or actions taken to mitigate its spread and other restrictions resulting from political instability and conflict, the integrity of data from

our trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our future clinical trials, which could cause us to reprioritize our clinical trials and use of funds for such trials, prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

The design or execution of our ongoing and future clinical trials may not support marketing approval or commercialization.

The design or execution of a clinical trial can determine whether its results will support marketing approval and successful commercialization, and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced. Additionally, in some instances, there can be significant variability in safety or efficacy results between different trials with the same product candidate due to numerous factors, including differences in trial protocols, size and type of the patient populations, variable adherence to the dosing regimen or other protocol requirements and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we conduct will demonstrate consistent or adequate efficacy and safety to obtain marketing approval to market our product candidates, or commercial acceptance thereafter. For example, we have designed our product candidates to be selective, but they may not be selective enough to achieve the desired safety or efficacy to gain marketing approval.

The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether marketing approval will be obtained for any of our product candidates. Our product candidates may not be approved even if they achieve their primary endpoints in future Phase 3 clinical trials or registrational trials. The FDA or comparable foreign regulatory authorities may disagree with our trial designs and our interpretation of data from preclinical studies or clinical trials. In addition, any of these regulatory authorities may change the requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 or registrational clinical trial. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or comparable foreign regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates, if approved.

We intend to develop certain of our product candidates and potentially other product candidates in combination with other therapies, which exposes us to additional risks.

We intend to develop certain of our product candidates and likely other future product candidates in combination with one or more other approved or unapproved therapies to treat cancer or other diseases. For example, in the fourth quarter of 2021, we announced that we had entered into a clinical trial supply agreement with Roche for our planned Phase 2a trial of GB1211 in combination with atezolizumab, a PD-L1 checkpoint inhibitor, for the first-line treatment of NSCLC. For instance, in the dose selection phase of our Phase 2a GALLANT-1 trial for the first-line treatment of NSCLC, we observed two serious adverse events of autoimmune-type skin rashes (showing perivascular lymphocytic infiltrates), which were determined by the principal investigator to be related to the administration of atezolizumab. The reactions were similar to those observed with atezolizumab and described in the label. Both reactions responded to therapy with oral glucocorticosteroids and were clinically manageable. In accordance with the protocol, we reduced the GB1211 dose to 100mg twice daily for the second patient cohort. Recruitment in this cohort is currently ongoing. Interestingly, inflammatory and perivascular lymphocytic infiltrates were observed in both skin reactions, and could signal an exaggerated immune activation, something often observed with checkpoint inhibitor therapy and associated with improved clinical outcomes. Because a central aspect of the mechanism of action for GB1211 in combination with a checkpoint inhibitor is to remove galectin-3 from the lymphocytes and the tumor cells, and thereby increase lymphocyte based tumor killing, we believe this could be a positive signal of enhanced lymphocyte activation. Although we may be able to observe activity of our product candidates as a monotherapy, it may be difficult to observe activity of our product candidates when administered with approved agents or investigational products. For example, based on an interim review of unblinded safety and efficacy data by a DSMB, the addition of GB0139 to nintedanib or pirfenidone was determined to potentially give rise to side effects that were not anticipated based on preclinical studies or early clinical studies in which GB0139 was given as a monotherapy, and, as a result, we modified our ongoing Phase 2b clinical for GB0139 to remove combination therapy. Such discoveries may lead to discontinuations of certain dosing groups and the modification or termination of our clinical trials. We are unable to predict how the results of our combination therapy trial cohorts could affect the prospects for securing marketing approval of GB0139 or commercial acceptance thereafter.

Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or comparable foreign regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in

combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

We also may choose to evaluate our current product candidates or any other future product candidates in combination with one or more cancer therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell our current product candidates or any product candidate we develop in combination with an unapproved cancer therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved cancer therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

If the FDA or comparable foreign regulatory authorities do not approve these other products or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the products we choose to evaluate in combination with our product candidate we develop, we may be unable to obtain approval of or market such combination therapy.

We have obtained orphan drug designation for GB0139; however, we may be unable to maintain this designation or obtain orphan drug designation for our other fibrosis or oncology product candidates, and we may not be able to realize the benefits of such designation, including potential marketing exclusivity of our product candidates, if approved.

As part of our business strategy, we sought and have received orphan drug designation from the FDA and the EC for treatment of IPF for GB0139; however, we may not be able to maintain this status. We may also seek orphan drug designation for future product candidates, and we may be unsuccessful in obtaining this designation. Regulatory authorities in some jurisdictions, including the United States and other major markets, may designate drugs intended to treat conditions or diseases affecting relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals annually 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. 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.

Similarly, in Europe, the EC grants orphan drug designation after receiving the opinion of the EMA Committee for Orphan Medicinal Products on an orphan drug designation application. Orphan drug designation is intended to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in Europe and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in Europe would be sufficient to justify the necessary investment in developing the drug. In Europe, orphan drug designation entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or EMA from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug or biologic no longer meets the criteria for orphan drug designation or if the drug or biologic is sufficiently profitable such that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even though we have obtained orphan drug designation for GB0139, and even if we are able to obtain orphan drug exclusivity for a future product candidate, that exclusivity may not effectively protect the relevant product candidate from competition because different therapies can be approved for the same condition and the same therapies can be approved for different conditions but used off-label for the orphan disease. Even after an orphan drug is approved, the FDA may subsequently approve another product for the same condition if the FDA concludes that the latter product is not the same product or is clinically superior to the protected orphan drug because it is shown to be safer or more effective or makes a major contribution to patient care. The FDA may reevaluate its regulations and policies under the Orphan Drug Act. We do not know if, when, or how the FDA

may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the orphan indication for which it was designated. Moreover, 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 if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. 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. While we have obtained orphan drug designation for GB0139, we may not be able to maintain such designations; and while we may seek orphan drug designation for applicable indications for any future product candidates, we may never receive such designations. Even though we have received such designations for GB0139, and may receive further such designations in the future, there is no guarantee that we will enjoy the benefits of those designations.

Breakthrough Therapy designation and Fast Track designation by the FDA, neither of which has been obtained, even if granted for any of our current or future product candidates, may not lead to a faster development or regulatory review process, and such designations do not increase the likelihood that any of our product candidates will receive marketing approval in the United States.

We intend to evaluate regulatory strategies that could enable us to take advantage of expedited development pathways for certain of our product candidates, although we cannot be certain that our product candidates will qualify for any expedited development pathways or that regulatory authorities will grant, or allow us to maintain, the relevant designations. Potential expedited development pathways that we could pursue include breakthrough therapy and Fast Track designation.

Breakthrough Therapy designation is intended to expedite the development and review of product candidates that are designed to treat serious or life-threatening diseases when 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. The designation of a product candidate as a breakthrough therapy provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate and ensure collection of appropriate data needed to support approval; more frequent written correspondence from FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review.

Fast Track designation is designed for product candidates intended for the treatment of a serious or life-threatening disease or condition, where nonclinical or clinical data demonstrate the potential to address an unmet medical need for this disease or condition. The designation of a product candidate as Fast Track provides potential benefits that include more opportunities for frequent interaction and communication with FDA during product development and eligibility for rolling review and priority review.

Even if we believe a particular product candidate is eligible for Breakthrough Therapy or Fast Track designation, we cannot assure you that the FDA would decide to grant such a designation in response to our written requests. Breakthrough Therapy designation and Fast Track designation do not change the standards for product approval, and there is no assurance that such designation will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the Breakthrough Therapy designation or Fast Track designation. Thus, even if we do receive Breakthrough Therapy or Fast Track designation for any of our product candidates, we may not experience a faster development process, review or marketing approval compared to conventional FDA procedures. The FDA may withdraw Breakthrough Therapy or Fast Track designation if it believes that the product no longer meets the qualifying criteria. Our business may be harmed if we are unable to avail ourselves of these or any other expedited development and regulatory pathways.

We currently conduct and may in the future conduct clinical trials for our product candidates outside the United States. The FDA, EMA or comparable foreign regulatory authorities may not accept data from such trials, and doing so subjects us to the risk that clinical development of our product candidates may be adversely affected by changes in local and regional political and economic conditions.

All of our ongoing clinical trials are enrolling or will seek to enroll some or all patients outside of the United States. The acceptance of trial data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authorities may be subject to certain conditions or may not be accepted at all. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed by clinical investigators of recognized competence 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 an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies 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, EMA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any comparable regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

In particular, we are seeking to enroll and have enrolled patients in our clinical trials in Ukraine, Russia and other Eastern European countries. Any escalation of political tensions, economic instability, military activity or civil hostilities in this region could disrupt or delay such trials, or adversely affect the timeliness of such trials. In connection with this geopolitical instability , the United States and other countries have imposed sanctions against Russia. Our ability to conduct these trials is dependent upon whether or not our involvement in such projects is restricted under U.S. or EU sanctions laws and the extent to which any of our current or prospective operations may become subject to those laws. Those laws may change from time to time, and any expansion of sanctions against Russia could hinder our ability to conduct such trials, which would result in the need for alternative trial sites, which would be costly and time-consuming and delay the clinical development of our product candidates.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates progress through preclinical to late-stage clinical trials to marketing approval and commercialization, various aspects of the development program, such as manufacturing methods and the product's formulation, may be altered along the way in an effort to optimize yield, manufacturing batch size, minimize costs and achieve consistent quality and results. These changes carry the risk that they will not achieve their intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of our current clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates and generate revenue.

In addition, there are risks associated with process development and large-scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we obtain marketing approval for any of our product candidates, there is no assurance that our third-party manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. Additionally, if we advance a biological candidate into IND-enabling studies, the manufacturing processes for biological products are more complex and expensive than with small molecule products and additional manufacturing suppliers may be needed to manufacture clinical supplies for these programs. If our contract manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We may not be successful in our efforts to identify or discover additional product candidates in the future.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our inability to design such product candidates with the pharmacological properties that we desire or attractive pharmacokinetics;
- our inability to design and develop a suitable manufacturing process; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Due to our limited resources and access to capital, we must make decisions on the allocation of resources to certain programs and product candidates; these decisions may prove to be wrong and may adversely affect our business.

We have limited financial and human resources and intend to initially focus on research programs and product candidates for a limited set of indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. In addition, we may seek to accelerate our development timelines, including by modifying the designs of ongoing or planned clinical trials or initiating certain clinical trials of our product candidates before earlier-stage studies have been completed. This approach may cause us to commit significant resources to prepare for and conduct later-stage trials for one or more product candidates that subsequently fail earlier-stage clinical testing. Therefore, our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities or expend resources on product candidates that are not viable.

There can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful.

If product liability lawsuits are brought against us, we may incur substantial financial or other liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of testing GB0139 and any of our other fibrosis or oncology product candidates in clinical trials and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense of these claims would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- inability to bring a product candidate to the market;
- decreased demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- fines, injunctions or criminal penalties;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate, if approved; and
- decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We will need to obtain additional insurance

for clinical trials as GB0139, and any of our other fibrosis or oncology product candidates continue clinical development and as additional product candidates enter the clinic. However, we may be unable to obtain, or may obtain on unfavorable terms, clinical trial insurance in amounts adequate to cover any liabilities from any of our clinical trials. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

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

The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major biotechnology and biopharmaceutical companies, specialty biotechnology and biopharmaceutical companies, and other biotechnology and biopharmaceutical companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large biotechnology and biopharmaceutical companies that are currently pursuing the development of products for the treatment of the biological processes that drive fibrosis and certain cancers. Companies that we are aware of that are targeting the treatment of various fibrosis indications include large companies with significant financial resources such as Pharmaxis Ltd, Biogen, Inc., AbbVie Inc., Gilead Sciences, Inc., Pliant Therapeutics, Inc., Galectin Therapeutics, Inc., FibroGen, Inc., Liminal BioSciences, Inc., Galapagos NV, Bristol Myers Squibb Co., Madrigal Pharmaceuticals, Inc., Inventiva, Akero Therapeutics, Inc., Boehringer Ingelheim, Roche/Genentech and Novartis AG. However, we know of no other companies currently in clinical development with an inhaled or orally available small molecule inhibitor of galectin-3 or an orally available small molecule inhibitor of LOXL2 for myelofibrosis. For additional information regarding our competition, see "*Business—Competition*."

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do.

Mergers and acquisitions in the biopharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient, or less expensive than any products that we may develop. Furthermore, products currently approved for other indications could be discovered to be effective treatments of the biological processes that drive fibrosis as well, which could give such products significant regulatory and market timing advantages over GB0139 or other fibrosis product candidates that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete and we may not be successful in marketing any product candidates we may develop against competitors. The availability of competitive products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Risks Related to Marketing, Reimbursement, Healthcare Regulations and Ongoing Regulatory Compliance

Even if a product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if GB0139 or any other fibrosis or oncology product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, such as Medicare and Medicaid programs and managed care organizations, and others in the medical community. In addition, the availability of coverage by third-party payors may be affected by existing and future health care reform measures designed to reduce the cost of health care. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages of our current or future product candidates compared to alternative treatments;
- limitations or warnings contained in the labeling approved for our current or future product candidates by the FDA or other applicable regulatory authorities;
- the clinical indications for which our current or future product candidates are approved;
- availability of alternative treatments already approved or commercially launched in the future;
- the ability to offer our products, if approved, for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the recommendations with respect to our product candidates in guidelines published by various scientific organizations applicable to us and our product candidates;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party coverage and adequate reimbursement; and
- the prevalence and severity of any side effects.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our products are safe, therapeutically effective and cost effective as compared with competing treatments. If any product candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that product candidate and may not become or remain profitable. If government and other third-party payors do not provide coverage and adequate reimbursement levels for any products we commercialize, market acceptance and commercial success would be reduced.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates profitably.

In the United States and in other countries, patients who are prescribed treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States, sales of any products for which we may receive regulatory marketing approval will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities such as Medicare, Medicaid, TRICARE, and the Veterans Administration, managed care providers, private health insurers, and other organizations. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Patients are unlikely to use our product candidates unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. See the section entitled, "*Business – Government Regulation – Coverage and Reimbursement.*"

Government authorities and other third-party payors decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

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

Our ability to commercialize any products successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government health care programs and private health insurers. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates, once approved. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates, if approved.

The MMA established the Medicare Part D program to provide a voluntary prescription drug and biologic benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs and biologics. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs and biologics, and each drug plan can develop its own formulary that identifies which drugs and biologics it will cover, and at what tier or level. However, Part D prescription drug formularies must include products within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs and biologics in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs and biologics may increase demand for products for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

Changes to these current laws and state and federal healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant

delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell any products for which we obtain regulatory approval, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we expect to establish a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop and for which we receive regulatory approval ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Our relationships with healthcare providers, physicians, prescribers, purchasers, third-party payors, charitable organizations and patients will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of biotechnology and biopharmaceutical products. Arrangements with third-party payors and customers can expose biotechnology and biopharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute, or AKS, and the federal False Claims Act, or FCA, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute biotechnology and biopharmaceutical products. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. See the section entitled, *"Business — Government Regulation — Other Healthcare Laws*".

The distribution of biotechnology and biopharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of biotechnology and biopharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from other aspects of its business.

It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, reputational harm, possible exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting of our operations, as well as 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. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Any action for violation of these laws, even if successfully defended, could cause a biotechnology and biopharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

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

If any of our product candidates are approved, they will be subject to ongoing post-marketing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with current good manufacturing practice, or cGMP, for any drug products we distribute and with good clinical practice, or GCP, requirements for any clinical trials that we conduct post-approval.

Manufacturers and their facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable tracking and tracing requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration. For example, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, sponsors of approved drugs and biologics must provide 6 months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed.

Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials 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 our products, withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and

- consent decrees or injunctions or the imposition of civil or criminal penalties.

Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is not inconsistent with the labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA and of other regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example, changes to our manufacturing arrangements; additions or modifications to product labeling; the recall or discontinuation of our products; or additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability. See the section entitled, "*Business — Government Regulation — Current and Future Healthcare Reform Legislation*".

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biologic 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. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Additionally, we expect to experience pricing pressures in connection with the sale of any future approved product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

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

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018, the U.S. government has shut down several times, and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC, and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to review and process our regulatory submissions timely, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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

EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European member states.

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, the recent U.K. referendum on its membership in the EU resulted in a majority of U.K. voters voting to exit the European Union, often referred to as Brexit. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the U.K. determines which EU laws to replicate or replace. If the U.K. were to significantly alter its regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs. As a result, Brexit could impair our ability to transact business in the European Union and the U.K. Market acceptance and sales of our product candidates will also depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

Much like the AKS prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to reward improper performance generally is governed by the national anti-bribery laws of the EU Member States, and in respect of the U.K. (which is no longer a member of the EU), the Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the U.K. despite its departure from the EU.

Payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including the EEA, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be

required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biotechnology and biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States, and generally, prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected.

We may incur substantial costs in our efforts to comply with evolving global data protection laws and regulations, and any failure or perceived failure by us to comply with such laws and regulations may harm our business and operations.

The global data protection landscape is rapidly evolving, and we may be or become subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, transfer, security and processing of personal data, such as information that we collect about participants and healthcare providers in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, which may create uncertainty in our business, affect our or our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal data, result in liability or impose additional compliance or other costs on us. Any failure or perceived failure by us to comply with federal, state, or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. California passed the California Data Privacy Protection Act of 2018, or the CCPA, which went into effect in January 2020, and was recently amended by the California Privacy Rights Act, which became effective on January 1, 2023, provides new data privacy rights for consumers and new operational requirements for companies, which may increase our compliance costs and potential liability. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. 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. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact certain of our business activities. The CCPA may lead to similar laws in other U.S. states or at a national level, which could increase our potential liability and adversely affect our business.

Additionally, a California ballot initiative, the California Privacy Rights Act, or the CPRA, was passed in November 2020 and became effective January 1, 2023. The CPRA imposes additional obligations on companies covered by the legislation and significantly modifies the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA.

Certain other state laws impose similar privacy obligations and we also expect that more states may enact legislation similar to the CCPA, which provides consumers with new privacy rights and increases the privacy and security obligations of entities handling certain personal information of such consumers. The CCPA has prompted a number of proposals for new federal and state-level privacy legislation. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies.

In addition, on March 2, 2021, Virginia enacted the Consumer Data Protection Act, or the CDPA, which became effective on January 1, 2023. The CDPA regulates how businesses (which the CDPA refers to as "controllers") collect and share personal information. While the CDPA incorporates many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of controllers. The law impacts how controllers collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests.

Also, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act, or the CPA, into law. The CPA will become effective on July 1, 2023. The CPA is rather similar to Virginia's CPDA but also contains additional requirements. The new measure applies to companies conducting business in Colorado or who produce or deliver commercial products or services intentionally targeted to its residents of the state that either: (1) control or process the personal data of at least 100,000 consumers during a calendar year; or (2) derive revenue or receive a discount on the price of goods or services from the sale of personal data and process or control the personal data of at least 25,000 consumers.

With the CPA, Colorado became the third state to enact a comprehensive privacy law but it is quite possible that other states will follow suit. The existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

In addition to our operations in the United States, which may be subject to healthcare and other laws relating to the privacy and security of health information and other personal information, we have operations in Europe and are subject to European data privacy laws, regulations and guidelines. The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to the EU GDPR and similar processing of personal data regarding individuals in the U.K. is subject to the U.K. GDPR and the U.K. Data Protection Act 2018.The GDPR is wide-ranging and imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside the EEA, including to the United States, providing details to those individuals regarding the processing of their personal health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, keeping personal information secure, having data processing agreements with third parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR increases substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20 million (£17.5 million) or up to 4% of our total worldwide annual turnover, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers.

Further, national laws of member states of the EU are in the process of being adapted to the requirements under the GDPR, thereby implementing national laws which may partially deviate from the GDPR and impose different obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EEA. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty. In addition, further to the U.K.'s exit from the EU on January 31, 2020, the GDPR ceased to apply in the U.K. at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the U.K.'s European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain U.K. specific amendments) into U.K. law, referred to as the U.K. GDPR. The U.K. GDPR and the U.K. Data Protection Act 2018 set out the U.K.'s data protection regime, which is independent from but aligned to the EU's data protection regime. The U.K. Government has announced plans to reform its data protection legal framework in the Data Reform Bill, but those have been put on hold. Non-compliance with the U.K. GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the U.K. is regarded as a third country under the EU's GDPR, the EC has now issued a decision recognizing the U.K. as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the U.K. remain unrestricted. Like the EU GDPR, the U.K. GDPR restricts personal data transfers outside the U.K. to countries not regarded by the U.K. as providing adequate protection. To enable the transfer of personal data outside of the EEA or the U.K., adequate safeguards must be implemented in compliance with European and U.K. data protection laws. On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EEA (or otherwise subject to the EU GDPR) to controllers or processors established outside the EEA (and not subject to the EU GDPR). The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the EU Data Protection Directive. The U.K. is not subject to the EC's new standard contractual clauses but has published its own version of standard clauses, referred to as "International Data Transfer Agreement" which entered into force on March 21, 2022 and enables transfers originating from the U.K. Transfers made pursuant to these new mechanisms need to be assessed on a case-by-case basis to ensure the law in the recipient country provides "essentially equivalent" protections to safeguard the transferred personal data as the EEA, and businesses are required to adopt supplementary measures if such standard is not met. We will be required to implement these new safeguards when conducting restricted data transfers under the EU and U.K. GDPR and doing so will require significant effort and cost.

In addition to the GDPR, the European Union is also in the process of replacing the e-Privacy Directive (2002/58/EC) with a new set of rules taking the form of a regulation, which will be directly implemented in the laws of each European member state, without the need for further enactment. Originally planned to be adopted and implemented at the same time as the GDPR, the ePrivacy Regulation is still going through the European legislative process. Draft regulations were rejected by the Permanent Representatives Committee of the Council of EU on November 22, 2019; it is not clear when new regulations will be adopted. Preparing for and complying with the GDPR and the ePrivacy Regulation (if and when it becomes effective) has required and will continue to require us to incur substantial operational costs and may require us to change our business practices. Despite our efforts to bring practices into compliance with the GDPR and before the effective date of the ePrivacy Regulation, we may not be

successful either due to internal or external factors such as resource allocation limitations. Non-compliance could result in proceedings against us by governmental entities, customers, data subjects, consumer associations or others.

We are conducting clinical trials in the EEA, and the GDPR increases our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we are required to have in place additional mechanisms and safeguards to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR is a rigorous and time-intensive process that increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. We expect that we will continue to face uncertainty as to whether our efforts to comply with any obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or biotechnology and biopharmaceutical partners. We may also experience hesitancy, reluctance, or refusal by European or multi-national vendors or biotechnology and biopharmaceutical partners to continue to use our products due to the potential risk exposure as a result of the current (and, in particular, future) data protection obligations imposed on them by certain data protection authorities in interpretation of current law, including the GDPR. Such vendors or biotechnology and biopharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain, or otherwise objectionable and therefore decide not to do business with us. Any of the forgoing could materially harm our business, prospects, financial condition and results of operations.

Legal, political and economic uncertainty surrounding the exit of the U.K. from the EU may be a source of instability in international markets, create significant currency fluctuations, adversely affect our operations in the U.K. and pose additional risks to our business, revenue, financial condition, and results of operations.

The U.K. formally left the EU on January 31, 2020, and the EU and the U.K. have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA provides details on how some aspects of the U.K. and EU's relationship will operate going forward however there are still many uncertainties and how the TCA will take effect in practice is still largely unknown. This lack of clarity on future U.K. laws and regulations and their interaction with the EU laws and regulations may negatively impact foreign direct investment in the U.K., increase costs, depress economic activity and restrict access to capital.

The uncertainty concerning the U.K.'s legal, political and economic relationship with the EU after Brexit may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise) beyond the date of Brexit.

These developments may have a significant adverse effect on global economic conditions and the stability of global financial markets and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

In addition, if other EU Member States pursue withdrawal, barrier-free access among the EEA overall could be diminished or eliminated. The long-term effects of Brexit will depend on how the terms of the TCA take effect in practice and any further agreements (or lack thereof) between the U.K. and the EU.

Such a withdrawal from the EU is unprecedented, and it is unclear how the restrictions on the U.K.'s access to the European single market for goods, capital, services and labor within the EU, or single market, and the wider commercial, legal and regulatory environment, will impact our current and future operations (including business activities conducted by third parties and contract manufacturers on our behalf) and clinical activities in the U.K. In addition to the foregoing, our U.K. operations support our current and future operations and clinical activities in the EU and EEA, and these operations and clinical activities could be disrupted by Brexit.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. The U.K. will lose the benefits of global trade agreements negotiated by the EU on behalf of its members, which may result in increased trade barriers that could make our doing business in the EU and the EEA more difficult. Since the regulatory framework in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime with respect to the approval of our product candidates in the U.K. now that the U.K. legislation can diverge from EU legislation. For instance, Great Britain will now no longer be covered by the centralized procedures for obtaining

EEA-wide marketing and manufacturing authorizations from the EMA (under the Northern Irish Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland) and a separate process for authorization of drug products will be required in Great Britain, resulting in an authorization covering the U.K. or Great Britain only. 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 the U.K. and/or the EU 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 U.K. and/or EU for our product candidates, which could significantly and materially harm our business. Even prior to any change to the U.K.'s relationship with the EU, the announcement of Brexit has created economic uncertainty surrounding the terms of Brexit, and its consequences could adversely impact customer confidence resulting in customers reducing their spending budgets on our product candidates, if approved, which could adversely affect our business, financial condition, results of operations and could adversely affect the market price of our common stock.

Additional laws and regulations governing international operations, and the complexity associated with maintaining geographically diverse operations, could negatively impact or restrict our operations and ability to grow.

We have offices and operations in six cities and in five countries. If we are unable to manage the risks of our global operations, including the potential for fluctuations in foreign exchange and inflation rates, international hostilities, the need for our executives to travel internationally, natural disasters, security breaches, failure to maintain compliance with internal control requirements and multiple legal and regulatory systems, our results of operations and ability to grow could be materially adversely affected.

We must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The U.S. Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business entity from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the biotechnology and biopharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals and healthcare providers in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information products classified for national security purposes, as well as certain products, technology and technical data relating to those products. As we expand our operations throughout the world, we will be required to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC may also suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

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

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

Risks Related to Our Intellectual Property

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

Our business will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, synthetic intermediates, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities and whether a court would issue an injunctive remedy. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. The patenting process is subject to numerous risks and there can be no assurance that we will be successful in obtaining patents for which we have applied. In addition, we may not pursue, obtain, or maintain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and biopharmaceutical fields involves complex legal and scientific questions and can be uncertain. The patent applications that we own, or in-license, may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our technology, including our product candidates, or prevent others from designing around the claims in our patents. If the breadth or strength of protection provided by the patent applications, we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

We cannot be certain that we were the first to file any patent application related to our technology, including our product candidates, and, if we were not, we may be precluded from obtaining patent protection for our technology, including our product candidates.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Similarly, for U.S. applications in which at least one claim is not entitled to a priority date before March 16, 2013, derivation proceedings can be instituted to determine whether the subject matter of a patent claim was derived from a prior inventor's disclosure.

We may be required to disclaim part or all of the term of certain patents. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent or patent application claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, would adequately protect our product candidates, or would be found by a court to be infringed by a competitor's technology or product. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products that have the same effect as our products on an independent basis and that do not infringe our patents or other intellectual property rights or will design around the claims of patents that may issue that cover our products.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or

the America Invents Act, after March 2013, the United States moved from a "first-to-invent" to a "first-inventor-to-file" system. Under a "first-inventor-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear, as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-inventor-to-file" provisions. In addition, the courts have yet to address many of these provisions and the applicability of the America Invents Act and new regulations on specific patents discussed herein, for which issues have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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 or use compounds that are similar to the compositions of our product candidates but that are not covered by the claims of our patents or those of our licensors;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications invented or developed using U.S. government funding, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;

- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or

- the patents of others may have an adverse effect on our business.

We may enter into license or other collaboration agreements in the future that may impose certain obligations on us. If we fail to comply with our obligations under such future agreements with third parties, we could lose license rights that may be important to our future business.

In connection with our efforts to expand our pipeline of product candidates, we may enter into certain licenses or other collaboration agreements in the future pertaining to the in-license of rights to additional product candidates. Such agreements may impose various diligence, milestone payment, royalty, insurance or other obligations on us. If we fail to comply with these obligations, our licensor or collaboration partners may have the right to terminate the relevant agreement, in which event we would not be able to develop or market the products covered by such licenses or agreements.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;

- the extent to which our product candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

- the sublicensing of patent and other rights under our collaborative development relationships;

- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

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

- the priority of invention of patented technology.

In addition, the agreements under which we may license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In addition, we may have limited control over the maintenance and prosecution of these in-licensed patents and patent applications, or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by any future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding, or defense activities may be less vigorous than had we conducted them ourselves.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be negatively impacted, and our business and competitive position would be harmed.

In addition to patent protection, we rely heavily upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take

against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts may be unwilling to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We also plan to adopt policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

Third-party claims of intellectual property infringement may be costly and time consuming to defend, and could prevent or delay our product discovery, development and commercialization efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and biopharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third-party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our product candidates and any license that is available may be non-exclusive, which could result in our competitors gaining access to the same intellectual property; and

- the need to redesign our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure.

Third parties may assert that we are employing their proprietary technology without authorization.

There may be third-party patents of which we are currently unaware with claims to compositions of matter, materials, formulations, methods of manufacture or methods for treatment that encompass the composition, use or manufacture of our product candidates. There may be currently pending patent applications of which we are currently unaware which may later result in issued patents that our product candidates or their use or manufacture may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patent were held by a court of competent jurisdiction to cover our product candidates, intermediates used in the manufacture of our product candidates or our materials generally, aspects of our formulations or methods of manufacture or use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, 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 our product candidates, which could harm our business significantly.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants 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 intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors

may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

Others may claim an ownership interest in our intellectual property, which could expose us to litigation and have a significant adverse effect on our prospects.

A third party may claim an ownership interest in one or more of our or our licensors' patents or other proprietary or intellectual property rights. A third party could bring legal actions against us and seek monetary damages and/or enjoin clinical testing, manufacturing and marketing of the affected product or products. While we are presently unaware of any claims or assertions by third parties with respect to our patents or other intellectual property, we cannot guarantee that a third party will not assert a claim or an interest in any of such patents or intellectual property. If we become involved in any litigation, it could consume a substantial portion of our resources and cause a significant diversion of effort by our technical and management personnel. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license to continue to manufacture or market the affected product, in which case we may be required to pay substantial royalties or grant cross-licenses to our patents. We cannot, however, assure you that any such license will be available on commercially acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product candidate or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights. Further, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree.

We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms.

Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently, and these rights may be held by others. We may develop products containing our compounds and pre-existing biotechnology and biopharmaceutical compounds. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established, or that have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, or challenging the patent rights of others, which could be expensive, time-consuming and unsuccessful.

Competitors or other third parties such as chemical and reagent suppliers may infringe our patents or the patents of our current or future licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question or for other reasons. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

We may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in an *ex-parte* re-examination, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office, or EPO, or other foreign patent offices. The costs of these opposition

proceedings could be substantial and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent offices then we may be exposed to litigation by a third-party alleging that the patent may be infringed by our product candidates or proprietary technologies.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent or first to file a patent application covering the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference or derivation proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference or derivation proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on our owned and in-licensed issued patents and patent applications are or will be due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. 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. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In certain circumstances, even inadvertent noncompliance events may permanently and irrevocably jeopardize patent rights. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Any patents, if issued, covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

If we or one of our licensors initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post-grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is

unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Our earliest patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could have a similar material adverse effect on our business, results of operations, financial condition and prospects.

Changes in patent law in the United States and in other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States or in other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 16, 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. On March 16, 2013, under the America Invents Act, enacted in September 2011, the United States transitioned to a "first-inventor-to-file" system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO on or after March 16, 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biotechnology and biopharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We have limited intellectual property rights outside of the United States and Europe and may not be able to protect and enforce our intellectual property rights throughout the world.

We have limited intellectual property rights outside the United States and Europe. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States and Europe can be less extensive than those in the United States and Europe. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States or laws in Europe. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or Europe, or from selling or importing products made using our inventions in and into the United States, Europe or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have

patent protection but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of, and may require a compulsory license to, patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology and biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

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

If we do not obtain patent term extension and data exclusivity or similar non-U.S. legislation extending the term of protection covering any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, also known as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failure to exercise due diligence during the testing phase or regulatory review process, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents, or otherwise failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

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

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Our Reliance on Third Parties

We rely and expect to continue to rely on third parties to conduct certain aspects of our ongoing and future preclinical studies and clinical trials, including investigator-sponsored clinical trials of our product candidates. If these third parties do not

successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.

We rely and expect to continue to rely on third parties to conduct certain aspects of our ongoing and future preclinical studies and clinical trials, under agreements with universities, medical institutions, clinical investigators, CROs, strategic collaborators and others. We expect to have to negotiate budgets and contracts with such third parties, which may result in delays to our development timelines and increased costs.

We will rely especially heavily on third parties over the course of our clinical trials, and, as a result, will have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities.

We may also rely on academic and private non-academic institutions and clinical investigators to conduct and sponsor clinical trials relating to our product candidates, such as the planned Phase 2 clinical trial of GB1211 in metastatic melanoma and HNSCC patients that will be sponsored by Providence Cancer Institute. We will not control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or foreign regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including due to elements of the design or execution of the trials or safety concerns or other trial results. Such arrangements will likely provide us certain information rights, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we would not have control over the timing and reporting of the data from investigator-sponsored trials, nor would we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the first-hand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

We and these third parties are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials conducted by third parties comply with the GCP requirements.

Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting aspects of our preclinical studies or clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our preclinical studies and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons or if, due to federal or state orders, they are unable to meet their contractual and regulatory obligations, our development timelines, including clinical development timelines, may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or other third parties terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms.

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 begins work. As a result, delays may occur, which can materially impact our ability to meet our desired 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.

We rely on third parties for materials, including tissue samples, required for our research and development activities, and if we are unable to reach agreements with these third parties, our research and development activities would be delayed.

We rely on third parties, primarily hospitals, health clinics and academic institutions, for the provision of tissue samples and other materials required in our research and development activities. Obtaining these materials requires various approvals as well as reaching a commercial agreement on acceptable terms with the hospital or other provider of the materials. While we currently have agreements in place with the institutions from which we receive our tissue samples, we do not have any exclusive arrangements with such sources, and there is no guarantee that we will be able to maintain or renew such agreements on commercially reasonable terms, if at all. If we were unable to maintain or renew such agreements, we would be forced to seek new arrangements with new hospitals, clinics or health institutions. If so, we may not be able to reach agreements with alternative partners or do so on terms acceptable to us. If we are unable to enter into such agreements, our research and development activities will be delayed and our ability to implement a key part of our development strategy will be compromised.

We contract with third parties for the manufacture of our product candidates for preclinical development, clinical testing, and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We rely on third-party contract manufacturers to manufacture our product candidates for preclinical studies and clinical trials. We do not own manufacturing facilities for producing any clinical trial product supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited or interrupted, or that they will be of satisfactory quality or continue to be available at acceptable prices. For example, the extent to which instability in geographies where we have operations or the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our product candidates will depend on whether broad-based sanctions continue for long term or escalate or if the economic challenges caused by the COVID-19 continue to impact supply chain, among many other factors. Any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to a back-up or alternative supplier, or we may not be able to transfer such skills or technology at all. Furthermore, a manufacturer may possess technology related to the manufacture of our product candidate that such manufacturer owns independently. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates.

In addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturer or manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for GB0139 or any other fibrosis or oncology product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third party

manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of an existing or future collaborator;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

We rely on a sole supplier or, in some cases, a limited number of suppliers for the manufacture of components of GB0139 and our other current fibrosis and oncology product candidates. If these suppliers are unable to supply necessary materials to us in the quantities we require, or at all, or otherwise default on their supply obligations to us, we may not be able to obtain alternative supplies from other suppliers on acceptable terms, in a timely manner, or at all. We also do not have long-term supply agreements with any of our suppliers. Our current contracts with certain suppliers may be canceled or not extended by such suppliers and, therefore, do not afford us with protection against a reduction or interruption in supplies. Moreover, in the event any of these suppliers breach their contracts with us, our legal remedies associated with such a breach may be insufficient to compensate us for any damages we may suffer.

In addition, we contract with fill and finishing providers with the appropriate expertise, facilities and scale to meet our needs. Failure to maintain cGMP can result in a contractor receiving FDA sanctions, which can impact our ability to operate or lead to delays in any clinical development programs. We believe that our current fill and finish contractor is operating in accordance with cGMP, but we can give no assurance that FDA or other regulatory agencies will not conclude that a lack of compliance exists. In addition, any delay in contracting for fill and finish services, or failure of the contract manufacturer to perform the services as needed, may delay any clinical trials, registration and launches, which could negatively affect our business. In the future, if we were to advance a biological product candidate into IND-enabling studies, we would need to identify and contract with suppliers who are able to produce biological product candidates and adhere to additional cGMP compliance obligations required for biologicals.

We may in the future seek to enter into collaborations with third parties for the development and commercialization of our product candidates, and our future collaborations will be important to our business. If we are unable to enter into collaborations, or if these collaborations are not successful, our business could be adversely affected.

A part of our strategy is to consider partnerships in indications and geographies where we believe partners can add significant commercial and/or development capabilities. Further, we have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we have entered and may in the future enter into collaborations with other companies to provide us with important technologies and funding for our programs and technology.

Any future collaborations we enter into may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

- collaborators may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;

- collaborators with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;

- collaborators may not provide us with timely and accurate information regarding development progress and activity under any future license agreement, which could adversely impact our ability to report progress to our investors and otherwise plan development of our product candidates;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and

- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If any future collaborations we enter into do not result in the successful discovery, development and commercialization of product candidates, if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under such collaboration. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

We face significant competition in seeking appropriate collaborators for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully establish a collaboration for one or more of our product candidates, potential collaborators must view these product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large biotechnology and biopharmaceutical companies that have resulted in a reduced number of potential future collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis,

on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into future collaborations or do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates, bring them to market and generate revenue from sales of drugs or continue to develop our technology, and our business may be materially and adversely affected. Even if we are successful in our efforts to establish new strategic collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic collaborations if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic collaboration agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

Risks Related to Managing Our Business and Operations

We may encounter difficulties in managing our growth, which could adversely affect our operations.

As of December 31, 2022, we had 45 full-time employees. As our clinical development and commercialization plans and strategies develop, and as we transition into operating as a public company, we will need to expand our managerial, clinical, regulatory, sales, marketing, financial, development, manufacturing and legal capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Our future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our development and commercialization efforts effectively, including the clinical and FDA review process for GB0139 and any other fibrosis or oncology product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

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

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including contract manufacturers and companies focused on research and development and discovery activities. There can be no assurance that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality, accuracy or quantity of the services provided is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain, or may be substantially delayed in obtaining, regulatory approval of our product candidates 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 not be able to successfully implement the tasks necessary to further develop and commercialize GB0139 or any other fibrosis or oncology product candidates and, accordingly, may not achieve our research, development and commercialization goals.

In December 2019, we acquired PharmAkea Inc., or PharmAkea, and may acquire additional technology and complementary businesses in the future. Acquisitions involve many risks, any of which could materially harm our business, including the diversion of management's attention from core business concerns, failure to effectively exploit acquired technologies, failure to successfully integrate the acquired business or realize expected synergies or the loss of key employees from either our business or the acquired businesses.

We have previously identified a material weakness in our internal control over financial reporting, which has since been remediated. If we experience future material weaknesses or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately report our financial condition or results of operations.

In connection with our preparation and the audits of our financial statements as of and for the years ended December 31, 2020 and 2019, we and our independent registered public accounting firm identified a material weakness as defined under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and by the Public Company Accounting Oversight Board (United States) in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis.

Our previous material weakness related to our financial statement closing process, primarily related to the lack of sufficient skilled personnel with U.S. generally accepted accounting principles, or U.S. GAAP, and Securities and Exchange Commission, or SEC, reporting knowledge and expertise for purposes of timely and reliable financial reporting and our dependence on third-party service providers for the preparation and closing of our financial records. Specifically, the material weakness identified related to the lack of appropriate internal controls over the work performed by the third-party service providers and that, as a result thereof, management failed to timely identify material misstatements in accounting for our debt and equity instruments, research and development, and taxation.

We have remediated the material weakness and have taken steps to strengthen our internal control over financial reporting, such as the hiring of Jonathan Freve as Chief Financial Officer in the second quarter of 2020 and a Corporate Controller in the fourth quarter of 2020. Additionally, we have designed and implemented a cross functional risk assessment process to identify and assess changes in the business that could significantly impact internal control over financial reporting. If, in the future, we identify further material weaknesses in our internal controls over financial reporting, we may not detect errors on a timely basis, and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company, we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Select Market or other adverse consequences that would materially harm our business. In addition, we could become subject to investigations by Nasdaq, the SEC, and other regulatory authorities, and become subject to litigation from investors and stockholders, which could harm our reputation and our financial condition, or divert financial and management resources from our core business.

An independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting in accordance with the provision of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, because no such evaluation has been required. Had an independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, material weaknesses may have been identified.

If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to develop current product candidates or identify and develop new product candidates will be impaired, could result in loss of markets or market share and could make us less competitive.

Our ability to compete in the highly competitive biotechnology and biopharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including Hans T. Schambye, M.D., Ph.D., our Chief Executive Officer and President, Anders Pedersen, our Chief Operating Officer, Bertil Lindmark, M.D., Ph.D., our Chief Medical Officer, Jonathan Freve, our Chief Financial Officer, and Stephanie Oestreich, our Chief Business Officer. The loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements could result in delays in product development and harm our business.

We conduct our operations globally from several locations including Denmark, the United States, Sweden, the U.K. and Canada. Competition for skilled personnel in our industry is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain with us, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development

teams may terminate their employment with us on short notice. Our key employees are at-will employees, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain "key person" insurance policies, but we may enter into such policies, on the lives of these individuals or the lives of certain of our employees. There is no guarantee that any "key person" insurance policy we may enter into would adequately compensate us for the loss of any key employee. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior scientific and medical personnel.

We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.

Our internal computer systems and those of any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, phishing or other unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, financial loss, a loss of our trade secrets or other proprietary information and damage to our reputation and otherwise negatively impact us. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. 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, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial of service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (*e.g.*, state breach notification laws), federal (*e.g.*, HIPAA, as amended by HITECH), and international (*e.g.*, the GDPR) law and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business.

We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyberattacks, and any such attacks could result in the losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business. By way of example, the CCPA, which went into effect on January 1, 2020, creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. 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. By way of example regarding foreign laws and regulations with respect to data privacy and security, the GDPR imposes strict requirements for processing the personal data of individuals in the EEA and U.K. 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 (£17.5 million) or 4% of the annual global revenues of the noncompliant company, whichever is greater.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from any such serious disaster.

Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or man-made accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Earthquakes or other natural disasters could further disrupt our operations and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event were to occur that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Portions of our future clinical trials may be conducted outside of the United States and unfavorable economic conditions resulting in the weakening of the U.S. dollar would make those clinical trials more costly to operate. Furthermore, the most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, including due to the economic challenges caused by the COVID-19 pandemic, could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or international trade disputes could also strain our suppliers, some of which are located outside of the United States, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our clinical development programs and the diseases our therapeutics are being developed to treat, and we intend to utilize appropriate social media in connection with our commercialization efforts following approval of our product candidates, if any. Social media practices in the biotechnology and biopharmaceutical industry continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities and heightened scrutiny by the FDA, the SEC and other regulators. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. If such disclosures occur, there is a risk that trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management, product candidates or products. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

The estimates of market opportunity and forecasts of market growth included in this Annual Report on Form 10-K or that we may otherwise provide may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all.

Market opportunity estimates and growth forecasts included in this Annual Report on Form 10-K or that we may otherwise provide are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be

accurate. The estimates and forecasts included in this Annual Report on Form 10-K relating to size and expected growth of our target market may prove to be inaccurate. Even if the markets in which we compete meet the size estimates and growth forecasts included in this Annual Report on Form 10-K, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties.

Our employees, independent contractors, consultants, commercial partners, collaborators and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners, collaborators and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws of the FDA and other similar foreign regulatory bodies, provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws will also increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. We have a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by our employees, independent contractors, consultants, commercial partners and vendors, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of civil, criminal and administrative penalties, damages, monetary fines, imprisonment, disgorgement, possible exclusion from participation in government 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, contractual damages, reputational harm, diminished profits and future earnings and the curtailment of our operations.

We use and generate materials that may expose us to material liability.

Our research programs involve the use of hazardous materials and chemicals, which are currently only handled by third parties. We are subject to foreign, federal, state and local environmental and health and safety laws and regulations governing, among other matters, the use, manufacture, handling, storage and disposal of hazardous materials and waste products such as human tissue samples that may have the potential to transmit diseases. We may incur significant costs to comply with these current or future environmental and health and safety laws and regulations. In addition, we cannot completely eliminate the risk of contamination or injury from hazardous materials and may incur material liability as a result of such contamination or injury. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our workers' compensation, property and business interruption insurance and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development activities involve the use of biological and hazardous materials and produce hazardous waste products. We or our CROs generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers' compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our products.

The Animal Welfare Act, or AWA, is the federal law that covers the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations that govern the humane handling, care, treatment and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size, and feeding, watering and shipping conditions. Third parties with whom we contract are subject to registration, inspections and reporting requirements under the AWA and comparable rules, regulations, and or obligations that may exist in many foreign jurisdictions. Furthermore, some states have their own regulations, including general anti-cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and/or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected.

Changes in U.S. tax law could adversely affect our financial condition and results of operations.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on March 27, 2020, President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act or the CARES Act, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. Future changes in U.S. tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisors regarding the implications of potential changes in U.S. tax laws on an investment in our common stock.

Unanticipated changes in effective tax rates or adverse outcomes resulting from examination of our income or other tax returns could expose us to greater than anticipated tax liabilities.

The tax laws applicable to our business, including the laws of Denmark, Sweden, the United States, and other jurisdictions, are subject to interpretation and certain jurisdictions may aggressively interpret their laws in an effort to raise additional tax revenue. The taxing authorities of the jurisdictions in which we operate may challenge our methodologies for valuing intercompany arrangements or our revenue recognition policies, which could increase our worldwide effective tax rate and harm our financial position and results of operations. It is possible that tax authorities may disagree with certain positions we have taken and any adverse outcome of such a review or audit could have a negative effect on our financial position and results of operations. Further, the determination of our worldwide provision for income taxes and other tax liabilities requires significant judgment by management, and there are transactions where the ultimate tax determination is uncertain. Although we believe that our estimates are reasonable, the ultimate tax outcome may differ from the amounts recorded in our consolidated financial statements and may materially affect our financial results in the period or periods for which such determination is made.

Our corporate structure and intercompany arrangements are subject to the tax laws of various jurisdictions, and we could be obligated to pay additional taxes, which would harm our results of operations.

Based on our current corporate structure, we are subject to taxation in several jurisdictions around the world with increasingly complex tax laws, the application of which can be uncertain. The amount of taxes we pay in these jurisdictions could increase substantially as a result of changes in the applicable tax principles, including increased tax rates, new tax laws or revised interpretations of existing tax laws and precedents. The authorities in these jurisdictions could review our tax returns or require us to file tax returns in jurisdictions in which we are not currently filing, and could impose additional tax, interest, and penalties. These authorities could also claim that various withholding requirements apply to us or our subsidiaries and assert that benefits of tax treaties are not available to us or our subsidiaries. The relevant taxing authorities may determine that the manner in which we operate our business does not achieve the intended tax consequences. If such a disagreement were to occur, and our position was not sustained, we could be required to pay additional taxes, interest, and penalties. Such authorities could claim that various withholding requirements apply to us or our subsidiaries or assert that benefits of tax treaties are not available to us or our subsidiaries. Any increase in the amount of taxes we pay or that are imposed on us could increase our worldwide effective tax rate.

Several countries in which we are located allow for tax incentives to attract and retain business. We have obtained incentives where available and practicable. Our taxes could increase if certain tax incentives are retracted, which could occur if we are unable to satisfy the conditions on which such incentives are based, if they are not renewed upon expiration, or if tax rates applicable to us in such jurisdictions otherwise increase. It is not anticipated that any material tax incentives will expire within the next year. However, due to the possibility of changes in existing tax law and our operations, we are unable to predict how any expirations will impact us in the future. In addition, acquisitions may cause our effective tax rate to increase, depending on the jurisdictions in which the acquired operations are located.

Certain of our subsidiaries may provide financing, products and services to, and may undertake certain significant transactions with, us or other of our subsidiaries in different jurisdictions. Several jurisdictions in which we operate have tax laws with detailed transfer pricing rules that require all transactions with non-resident related parties be priced using arm's length pricing principles, and that contemporaneous documentation must exist to support such pricing. There is a risk that the taxing authorities may not deem our transfer pricing documentation acceptable. In addition, the Organization for Economic Cooperation and Development continues to issue guidelines and proposals related to Base Erosion and Profit Shifting which may result in legislative changes that could reshape international tax rules in numerous countries and negatively impact our effective tax rate.

Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.

We have net operating loss carryforwards and tax credit carryforwards for U.S. federal and state income tax purposes which begin to expire in future years. Additionally, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50 percentage points within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Public offerings, private placements and other transactions that have occurred since our inception, may trigger such an ownership change pursuant to Section 382. Any such limitation, whether as the result of a prior public offering, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years. The reduction of the corporate tax rate under the Tax Cuts and Jobs Act of 2017, or the Tax Cuts and Jobs Act, may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us.

Risks Related to Our Common Stock

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors include:

- the commencement, enrollment or results of our current fibrosis- and oncology- focused Phase 2 clinical trials of GB0139, GB1211 and GB2064;
- any delay in identifying and advancing a clinical candidate for our other development programs;
- any delay in our regulatory filings for GB0139 or our other fibrosis or oncology product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including, without limitation, the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results or delays in future clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval of GB0139 or any other fibrosis or oncology product candidate;
- changes in laws or regulations applicable to GB0139 or any other fibrosis or oncology product candidate, including, but not limited to, clinical trial requirements for approvals;

- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- our failure to commercialize our product candidates, if approved;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of GB0139 or any other fibrosis or oncology product candidate;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or product candidates in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- changes in the structure of the healthcare payment systems;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for biotechnology and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including as a result of the COVID-19 pandemic. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. You may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has

often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources.

If our common stock is delisted from The Nasdaq Global Select Market, the liquidity of our common stock would be adversely affected and the market price of our common stock could decrease.

Our common stock is currently listed on The Nasdaq Global Select Market and closed at $2.20 on March 1, 2023. The Nasdaq Stock Market LLC, or Nasdaq, has minimum requirements that a company must meet in order to remain listed on Nasdaq markets, including that we maintain a minimum closing bid price of $1.00 per share. If we fail to maintain such minimum requirements and a final determination is made by Nasdaq that our common stock must be delisted, the liquidity of our common stock would be adversely affected and the market price of our common stock could decrease. Our failure to be listed on Nasdaq or another national securities exchange would have a material adverse effect on the value of your investment in us.

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

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Furthermore, future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

As of March 1, 2023, our executive officers, directors and their affiliates beneficially held, in the aggregate, approximately 21.9% of our outstanding voting stock. These stockholders, acting together, would be able to significantly influence all matters requiring stockholder approval. For example, these stockholders would be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

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

We are an EGC as defined in the JOBS Act, enacted in April 2012. For as long as we continue to be an EGC, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not EGCs, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, or Section 404, reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may remain an EGC until December 31, 2025, although circumstances could cause us to lose that status earlier. We will remain an EGC until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering, or IPO, (b) in which we have total annual gross revenue of at least $1.235 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting obligations by providing only two years of audited financial statements. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of 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.

Under the JOBS Act, EGCs can also delay adopting new or revised accounting standards until such time as those standards apply to private companies, which may make our financial statements less comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company," meaning that the market value of our shares held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) if the market value of our shares held by non-affiliates is more than $250 million but less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

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

As a public company, we incur, and we will continue to incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial reporting controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Recent legislation permits EGCs to implement many of these requirements over a longer period and up to five years from the pricing of our IPO. The costs associated with operating as a public company may decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products, if approved, or services. Additionally, stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis, and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an EGC, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an EGC for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

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

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the

inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

We have broad discretion in the use of our existing cash, cash equivalents and marketable securities and may not use them effectively.

Our management has broad discretion in the application of our existing cash, cash equivalents and marketable securities. Because of the number and variability of factors that will determine our use of our existing cash, cash equivalents and marketable securities, their ultimate use may vary substantially from their currently intended use. Our management might not apply our existing cash, cash equivalents and marketable securities in ways that ultimately increase the value of our common stock. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest our cash, cash equivalents and marketable securities in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply our cash, cash equivalents and marketable securities in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

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

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue convertible preferred stock on terms determined by the board of directors without stockholder approval and which convertible preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, or DGCL, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Our amended and restated bylaws will designate certain courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to litigate disputes with us in a different judicial forum.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (v) any action asserting a claim governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein, or the Delaware forum provision. The Delaware forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Unless we consent in writing to the selection of an alternate forum, the United States District Court for the District of Delaware shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the federal forum provision, as we are incorporated in the State of Delaware. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware forum provision and the federal forum provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder.

The Delaware forum provision and the federal forum provision may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware. In addition, these forum selection clauses in our bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our federal forum provision. The federal forum provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable or invalid, and if the federal forum provision is found to be unenforceable, we may also incur additional costs associated with resolving such matters. The Court of Chancery of the State of Delaware and the United States District Court for the District of Delaware may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Our issuance of additional capital stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

We expect to issue additional capital stock in the future that will result in dilution to all other stockholders. We expect to grant equity awards to employees, directors, and consultants under our stock incentive plans. We may also raise capital through equity financings in the future. As part of our business strategy, we may acquire or make investments in complementary companies, products, or technologies and issue equity securities to pay for any such acquisition or investment. Any such issuances of additional capital stock may cause stockholders to experience significant dilution of their ownership interests and the per share value of our common stock to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

As of December 31, 2022, the facilities that we lease are the following:

Location	Primary Use	Approximate Square Footage	Lease Expiration Date	Renewal Option
Ole Maaloes Vej 3, DK-2200 Copenhagen N, Denmark	Office space	4,000	January 31, 2025	None
Evergreen House North, Grafton Place, London, NW1 2DX	Office space	1,000	February 29, 2024	None
Sahlgrenska Science Park AB, Medicinaregatan 8A, 413 90 Gothenburg, Sweden	Office space	388	May 30, 2023	None
Stevenage Open Innovation Bioscience Park, Stevenage, Hertfordshire, SG1 2FX	Laboratory space	1,046	August 8, 2025	None

We believe that our current facilities are sufficient to meet our current and near-term needs and that, should it be needed, suitable additional space will be available.

Item 3. Legal Proceedings.

We are not party to any material legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business. We cannot predict the outcome of any such legal matters or claims, and despite the potential outcomes, the existence thereof may have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades on the Nasdaq Global Select Market under the symbol "GLTO" and has been publicly traded since October 29, 2020. Prior to that time, there was no established public trading market for our common stock.

Holders of Our Common Stock

As of March 1, 2023, we had 25,673,474 outstanding shares of common stock and no outstanding shares of preferred stock. At March 1, 2023, there were 27 holders of record of our common stock. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial holders represented by these record holders.

Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Recent Sales of Unregistered Securities

None.

Use of Proceeds from Registered Securities

On November 2, 2020, we completed our IPO in which we issued and sold 6,342,207 shares of common stock, $0.00001 par value per share, including 675,540 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock. The offer and sale of the shares in the IPO was registered under the Securities Act pursuant to registration statements on Form S-1 (File No. 333-249369), which was filed with the SEC on October 7, 2020 and subsequently amended and declared effective on October 28, 2020, or the Prospectus. The underwriters of the offering were BofA Securities, Inc., SVB Leerink LLC and Credit Suisse Securities (USA) LLC and Kempen & Co U.S.A, Inc.

We raised $86.3 million in net proceeds after deducting underwriting discounts and commissions of $6.7 million and other offering expenses of $2.1 million payable by us. No underwriting discounts and commissions or offering expenses were paid directly or indirectly to any of our directors of officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of December 31, 2022, $20.7 million of the net proceeds from our IPO have been used for general working capital purposes, including the funding of our clinical development programs. We have invested the unused net proceeds from the offering in money market accounts and marketable debt securities. We expect to use the net proceeds from the offering described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on October 30, 2020.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Reserved.

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

We are a clinical-stage biotechnology company developing novel small molecule therapeutics that are designed to target the biological processes that lie at the heart of cancer and fibrotic diseases. Our strategy is to focus on diseases without disease-modifying treatment options and where there is a high unmet medical need. We are concentrating on the development of a new class of medicines: small molecule inhibitors of galectin-3 and lysyl oxidase-like 2, or LOXL2, that target underlying biology for the treatment of multi-factorial diseases like cancer and fibrotic diseases.

Our most advanced product candidate, GB0139, is in Phase 2b clinical development and our other current fibrosis and oncology product candidates are in early stages of clinical development. Our ability to generate revenue from product sales sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Our operations to date have been financed primarily from our initial public offering, or IPO, the issuance of convertible preferred shares and convertible notes. Since inception, we have had significant operating losses. Our net loss was $61.6 million and $51.8 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $217.7 million and $66.1 million in cash, cash equivalents and marketable securities.

Galecto, Inc. was incorporated in Delaware in October 2019. Shares in Galecto Biotech AB, a Swedish operating company, were exchanged at a one-to-one ratio for shares in Galecto, Inc. in a common control/tax-free reorganization. As of December 31, 2022, the Company's wholly owned subsidiaries were PharmAkea, Inc., Galecto Securities Corporation and Galecto Biotech AB. Galecto ApS, a Danish operating company, was Galecto Biotech AB's wholly owned subsidiary.

Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our accounts payable and accrued expenses. We expect to continue to incur net losses for the foreseeable future, and we expect our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. In particular, we expect our expenses to increase as we continue our development of, and seek regulatory approvals for, our product candidates, as well as hire additional personnel, pay fees to outside consultants, lawyers and accountants, and incur other increased costs associated with being a public company. See "Item 1A. Risk Factors - Risks Related Our Financial Position and Need for Additional Capital - *We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future.*" In addition, if and when we seek and obtain regulatory approval to commercialize any product candidate, we will also incur increased expenses in connection with commercialization and marketing of any such product. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

Based upon our current operating plan, we believe that our existing cash, cash equivalents and marketable securities of $66.1 million as of December 31, 2022, will be sufficient to continue funding our development activities into the second half of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. To finance our operations beyond that point we will need to raise additional capital, which cannot be assured.

To date, we have not had any products approved for sale and, therefore, have not generated any product revenue. We do not expect to generate any revenues from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates.

The spread of COVID-19 and identification of new variants and subvariants of the virus has impacted the global economy and, both directly and indirectly, 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. The ongoing economic challenges of the COVID-19 pandemic and its effects on our business and operations are uncertain.

In addition, economic uncertainty in various global markets, including the U.S. and Europe, caused by political instability and conflict, such as the ongoing conflict in Ukraine, and economic challenges caused by the COVID-19 pandemic, have led to market disruptions, including significant volatility in commodity prices, credit and capital market instability and supply chain interruptions, which have caused record inflation globally. Our business, financial condition and results of operations could be materially and adversely affected by further negative impact on the global economy and capital markets resulting from these global economic conditions, particularly if such conditions are prolonged or worsen.

Although, to date, our business has not been materially impacted by these global economic and geopolitical conditions, it is impossible to predict the extent to which our operations will be impacted in the short and long term, or the ways in which such instability could impact our business and results of operations. The extent and duration of these market disruptions, whether as a result of the military conflict between Russia and Ukraine and effects of the Russian sanctions, geopolitical tensions, record inflation or otherwise, are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described in this report.

For additional information on the various risks posed by the COVID-19 pandemic and global economic uncertainty, please read the section entitled “Risk Factors” in this Annual Report on Form 10-K.

Components of Operating Results

Operating Expenses

Our operating expenses since inception have consisted primarily of research and development expenses and general and administrative costs.

Research and Development

Our research and development expenses consist primarily of costs incurred for the development of our product candidates and our drug discovery efforts, which include:

- personnel costs, which include salaries, benefits and equity-based compensation expense;
- expenses incurred under agreements with consultants, and third-party contract organizations that conduct research and development activities on our behalf;
- costs related to sponsored research service agreements;
- costs related to production of preclinical and clinical materials, including fees paid to contract manufacturers;
- laboratory and vendor expenses related to the execution of preclinical studies and planned clinical trials;
- laboratory supplies and equipment used for internal research and development activities; and
- acquired in-process research and development programs.

We expense all research and development costs in the periods in which they are incurred, including for acquired in-process research and development. Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

We have historically met the requirements to receive a tax credit in Denmark of up to $0.9 million per year for losses resulting from research and development costs of up to approximately $4.1 million per year. The tax credit is reported as a reduction to research and development expense in the consolidated statements of operations. We recorded a reduction to research and development expense of $0.8 million and $0.9 million for the year ended December 31, 2022 and 2021, respectively. The credits are available the following year, in 2023 and 2024, respectively.

Our direct research and development expenses are not currently tracked on a program-by-program basis. We use our personnel and infrastructure resources across multiple research and development programs directed toward identifying and developing product candidates. The majority of our clinical spending in the years ended December 31, 2022 and 2021 was on GB0139.

We expect to continue to incur research and development expenses for the foreseeable future as we continue to invest in research and development activities related to developing GB0139, GB2064, GB1211 and any other product candidates we may develop, including investments in conducting clinical trials, manufacturing and otherwise advancing our programs. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain.

Because of the numerous risks and uncertainties associated with product development and the current stage of development of our product candidates and programs, we cannot reasonably estimate or know the nature, timing and estimated costs necessary to complete the remainder of the development of our product candidates or programs. We are also unable to predict if, when, or to what extent we will obtain approval and generate revenues from the commercialization and sale of our product candidates. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, including:

- successful completion of preclinical studies and initiation of clinical trials for GB0139, our other current fibrosis and oncology product candidates and any future product candidates;
- successful completion of our ongoing Phase 2 clinical trials for GB0139, GB2064 and GB1211, and any clinical trials for future product candidates;
- data from our clinical programs that support an acceptable risk-benefit profile of our product candidates in the intended patient populations;
- acceptance by the FDA, regulatory authorities in Europe, Health Canada or other regulatory agencies of regulatory filings for GB0139, GB2064, GB1211 and any future product candidates;
- expansion and maintenance of a workforce of experienced scientists and others to continue to develop our product candidates;
- successful application for and receipt of marketing approvals from applicable regulatory authorities;
- obtainment and maintenance of intellectual property protection and regulatory exclusivity for our product candidates;
- arrangements with third-party manufacturers for, or establishment of, commercial manufacturing capabilities;
- establishment of sales, marketing and distribution capabilities and successful launch of commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies;
- obtainment and maintenance of coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;
- maintenance, enforcement, defense and protection of our rights in our intellectual property portfolio;
- avoidance of infringement, misappropriation or other violations with respect to others' intellectual property or proprietary rights; and
- maintenance of a continued acceptable safety profile of our products following receipt of any marketing approvals.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our preclinical studies and clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. A change in the outcome of any of these factors could mean a significant change in the costs and timing associated with the development of our current and future preclinical and clinical product candidates. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in execution of or enrollment in any of our preclinical studies or clinical trials, we could be required to expend significant additional financial resources and time on the completion of preclinical and clinical development.

Research and development activities account for a significant portion of our operating expenses. We expect our research and development expenses to continue for the foreseeable future as we continue to implement our business strategy, which includes advancing GB0139, GB2064 and GB1211 through clinical development and other product candidates further into clinical development, expanding our research and development efforts, including hiring additional personnel to support our research and development efforts, and seeking regulatory approvals for our product candidates that successfully complete clinical trials. In addition, product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect our research and development expenses to increase as our product candidates advance into later stages of clinical development. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development.

General and Administrative Expenses

Our general and administrative expenses consist primarily of personnel costs, depreciation expense and other expenses for outside professional services, including legal, human resources, audit and accounting services and facility-related fees not otherwise included in research and development expenses. Personnel costs consist of salaries, benefits and stock-based compensation expense, for our personnel in executive, finance and accounting, business operations and other administrative functions. We expect our general and administrative expenses to continue over the next several years to support our continued research and development activities, manufacturing activities, increased costs of expanding our operations and operating as a public company. These expenses will likely include increases related to the hiring of additional personnel, legal, regulatory and other fees, director and officer insurance premiums and investor relations costs associated with our growth and continued expansion of our operations.

Other Income (Expense), Net

Our other income (expense), net is comprised of:

- Interest income: The interest income earned on our cash, cash equivalents and marketable securities is recorded in our statements of operations.
- Gain (loss) on sales of marketable securities: The loss on the sales of our marketable securities are recorded in our statements of operations.
- Foreign exchange: The functional currency of our subsidiaries in Denmark and Sweden is the Euro. Transactions denominated in currencies other than the Euro result in exchange gains and losses that are recorded in our consolidated statements of operations.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following sets forth our results of operations for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Change	
	2022	2021	Amount	Percent
	(in thousands)			
Operating expenses				
Research and development	$ 48,206	$ 38,488	$ 9,718	25%
General and administrative	13,001	13,739	(738)	-5%
Total operating expenses	61,207	52,227	8,980	17%
Loss from operations	(61,207)	(52,227)	(8,980)	17%
Other income (expense), net	(417)	475	(892)	-188%
Net loss	$ (61,624)	$ (51,752)	$ (9,872)	19%

Research and development expenses

Research and development expenses were comprised of:

	Year Ended December 31,		Change
	2022	2021	
		(in thousands)	
Preclinical studies and clinical trial-related activities	$ 26,488	$ 17,358	$ 9,130
Chemistry, manufacturing and control	7,019	9,989	(2,970)
Personnel	9,331	7,383	1,948
Consultants and other costs	5,368	3,758	1,610
Total research and development expenses	$ 48,206	$ 38,488	$ 9,718

Research and development expenses were $48.2 million for the year ended December 31, 2022, compared to $38.5 million for the year ended December 31, 2021. The increase of $9.7 million was primarily related to an increase in clinical trial-related expenses of $9.1 million resulting from our four Phase 2 clinical trials, increased personnel costs due to additional headcount of $1.2 million and personnel costs for non-cash stock-based compensation of $0.7 million and increased other research and development costs of $1.6 million, offset by decreased chemistry, manufacturing and control, or CMC, activities of $2.9 million.

General and administrative expenses

General and administrative expenses were $13.0 million for the year ended December 31, 2022, compared to $13.7 million for the year ended December 31, 2021. The decrease of $0.7 million was primarily related to a decrease in consulting costs of $1.0 million and legal related costs of $0.7 million, offset by increased personnel costs of $0.6 million due to additional headcount as well as non-cash stock-based compensation of $0.4 million.

Other income (expense), net

Other expense was $(0.4) million for the year ended December 31, 2022, compared to other income of $0.5 million for the year ended December 31, 2021. The decrease of $0.9 million was due to an increase in net foreign exchange loss of $1.4 million and an increase in the loss on the sale of marketable securities of $0.1 million, offset by an increase in net interest income of $0.6 million.

Liquidity and Capital Resources

Sources of Liquidity

Our operations to date have been financed primarily through our IPO, the issuance of common stock through our at-the-market program and the issuance of convertible preferred shares and convertible notes. Since inception, we have had significant operating losses. On November 2, 2020, we completed our IPO in which we raised $86.3 million in net proceeds. On November 4, 2021, we filed with the SEC, and the SEC declared effective on November 12, 2021, a registration statement on

Form S-3, or the Registration Statement, which registers the offering, issuance and sale of up to $200.0 million of our common stock, preferred stock, debt securities, warrants, subscription rights and/or units of any combination thereof. Simultaneous with the filing of the Registration Statement, we entered into an Open Market Sale Agreement[SM] with Jefferies LLC, as sales agent, to provide for the issuance and sale of up to $50.0 million of our common stock from time to time in "at-the-market" offerings under the Registration Statement and related prospectus filed with the Registration Statement, or the ATM Program. During the quarter ended December 31, 2022, we sold an aggregate of 71,363 shares of our common stock under the ATM Program at a weighted average selling price of $1.62 per share. During the year ended December 31, 2022, we sold an aggregate of 390,560 shares of our common stock under the ATM Program at a weighted average selling price of $1.92 per share. We had no sales under the ATM Program during the year ended December 31, 2021.

Our net losses were $61.6 million and $51.8 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $217.7 million and $66.1 million in cash, cash equivalents and marketable securities. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Net cash used in operating activities	$ (42,932)	$ (52,308)
Net cash provided by (used in) investing activities	12,384	(48,048)
Net cash provided by financing activities	507	—
Net decrease in cash and cash equivalents	$ (30,041)	$ (100,356)

Net Cash Used in Operating Activities

Cash used in operating activities of $42.9 million during the year ended December 31, 2022 was attributable to our net loss of $61.6 million, offset by a net increase of $11.9 million in our working capital and in non-cash items of $6.8 million principally with respect to non-cash stock-based compensation, non-cash amortization of premiums and discounts on marketable securities and non-cash amortization of the right of use lease asset.

Cash used in operating activities of $52.3 million during the year ended December 31, 2021 was attributable to our net loss of $51.8 million together with a net decrease of $6.6 million in our working capital, offset by an increase in non-cash items of $6.1 million principally with respect to non-cash stock-based compensation and non-cash amortization of premiums and discounts on marketable securities.

Net Cash Used in Investing Activities

Cash provided by investing activities of $12.4 million for the year ended December 31, 2022 was attributable to $57.5 million in proceeds from the sale of marketable securities, offset by $44.9 million for the purchase of marketable securities and $0.2 million for the purchase of property and equipment.

Cash used in investing activities of $48.0 million for the year ended December 31, 2021 was attributable to $84.2 million for the purchase of marketable securities and $0.2 million for the purchase of property and equipment, offset by $36.4 million in proceeds from the sale of marketable securities.

Net Cash Provided by Financing Activities

Cash provided by financing activities of $0.5 million for the year ended December 31, 2022 was the result of net proceeds from the issuance of our common stock.

We had no cash used in or provided by financing activities for the year ended December 31, 2021.

Funding Requirements

Any product candidates we may develop may never achieve commercialization and we anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development expenses, general and administrative expenses, and capital expenditures will continue. As a result, until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses; costs related to third-party clinical research, manufacturing and development services; costs relating to the build-out of our headquarters and other offices, our laboratories and our manufacturing facility; license payments or milestone obligations that may arise; laboratory expenses and costs for related supplies; clinical costs; manufacturing costs; legal and other regulatory expenses and general overhead costs.

Based upon our current operating plan, we believe that our existing cash, cash equivalents and marketable securities of $66.1 million as of December 31, 2022 will be sufficient to continue funding our development activities into the second half of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. To finance our operations beyond that point we will need to raise additional capital, which cannot be assured. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Volatility in equity capital markets may adversely affect the market price of our equity securities, which may materially and adversely affect our ability to fund our business through public or private sales of equity securities. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders, will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

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. Our future funding requirements will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our product candidates, including GB0139, GB2064, GB1211 and any other product candidates we may develop in the future;
- the clinical development plans we establish for these product candidates;
- the number of, and development requirements for, other product candidates that we develop;
- the timelines of our clinical trials and the overall costs to finish the clinical trials due to geopolitical instability and conflict and economic challenges caused by the COVID-19 pandemic;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the European Medicines Agency, or EMA, and other comparable foreign regulatory authorities;
- our ability to enter into contract manufacturing arrangements for supply of active pharmaceutical ingredient, or API, and manufacture of our product candidates, and the terms of such arrangements;
- whether we are able to enter into and maintain collaboration agreements, including the terms of and timing of payments under any such agreements;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;

- the extent to which we acquire or in-license other products, product candidates, or technologies;
- the effect of competing clinical, technological and market developments;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities;
- changes in economic conditions, including rising inflation and interest rates, lower consumer confidence and volatile equity capital markets; and
- the costs of continuing to operate as a public company.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

Critical Accounting Policies and Significant Judgments and Estimates

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

Research and Development Costs

We incur substantial expenses associated with clinical trials. Accounting for clinical trials relating to activities performed by CROs, CMOs and other external vendors requires management to exercise significant estimates in regard to the timing and accounting for these expenses. We estimate costs of research and development activities conducted by service providers, which include, the conduct of sponsored research, preclinical studies and contract manufacturing activities. The diverse nature of services being provided under CRO and other arrangements, the different compensation arrangements that exist for each type of service and the lack of timely information related to certain clinical activities complicates the estimation of accruals for services rendered by CROs, CMOs and other vendors in connection with clinical trials. We record the estimated costs of research and development activities based upon the estimated amount of services provided by the CRO, CMOs and other vendors but not yet invoiced and include these costs in the accrued and other current liabilities or prepaid expenses on the balance sheets and within research and development expense on the consolidated statements of operations. In estimating the duration of a clinical study, we evaluate the start-up, treatment and wrap-up periods, compensation arrangements and services received attributable to each clinical trial and fluctuations are regularly tested against payment plans and trial completion assumptions.

We estimate these costs based on factors such as estimates of the work completed and budget provided and in accordance with agreements established with our collaboration partners and third-party service providers. We make significant judgments and estimates in determining the accrued liabilities and prepaid expense balances in each reporting period. As actual costs become known, we adjust our accrued liabilities or prepaid expenses. We have not experienced any material differences between accrued costs and actual costs incurred since our inception.

Our expenses related to clinical trials are based on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that may be used to conduct and manage clinical trials on our behalf. We generally accrue expenses related to clinical trials based on contracted amounts applied to the level of patient enrollment and activity. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis.

Stock-based Compensation

We have issued stock-based compensation awards through the granting of stock options, which generally vest over a four-year period. We account for stock-based compensation in accordance with ASC 718, *Compensation-Stock Compensation*, or ASC 718. In accordance with ASC 718, compensation cost is measured at estimated fair value and is recognized as compensation expense over the vesting period during which service is provided in exchange for the award.

We use a Black-Scholes option pricing model to determine fair value of our stock options. The Black-Scholes option pricing model includes various assumptions, including the fair value of common shares, expected life of stock options, the expected volatility based on the historical volatility of a publicly traded set of peer companies and the expected risk-free interest rate. These assumptions reflect our best estimates, but they involve inherent uncertainties based on market conditions generally outside our control. As a result, if other assumptions had been used, stock-based compensation cost could have been materially impacted. Furthermore, if we use different assumptions for future grants, share-based compensation cost could be materially impacted in future periods.

The fair value of our awards in the year ended December 31, 2022 has been estimated using Black-Scholes based on the following assumptions: term of 6.0 years; volatility of 90.0%; risk-free rate of 1.7%; and no expectation of dividends. The fair value of our awards in the year ended December 31, 2021 has been estimated using Black-Scholes based on the following assumptions: term of 6.0 years; volatility of 90.5%; risk-free rate of 0.7%; and no expectation of dividends

We will continue to use judgment in evaluating the assumptions utilized for our equity-based compensation expense calculations on a prospective basis. In addition to the assumptions used in the Black-Scholes model, the amount of equity-based compensation expense we recognize in our consolidated financial statements includes stock option forfeitures as they occurred. We recognize forfeitures as they occur, and the compensation expense is reversed in the period that the forfeiture occurs.

Income Taxes

Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, and operating losses and tax credit carry forwards. Deferred tax assets and liabilities are measured using enacted statutory tax rates expected to apply to taxable income in the jurisdictions and years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

Based on the level of historical operating results and projections for the taxable income for the future, we have determined that it is more likely than not that our net deferred tax assets will not be realized. Accordingly, we have recorded a full valuation allowance to reduce our deferred tax assets.

We recognize tax benefits from uncertain tax positions only if (based on the technical merits of the position) it is more likely than not that the tax positions will be sustained on examination by the tax authority. The tax benefits recognized in the financial statements from such positions are measured based on the largest amount that is more than 50% likely to be realized upon ultimate settlement. We have not recorded any uncertain tax positions as of December 31, 2022 or 2021. We do not believe there will be any material changes in our unrecognized tax positions over the next 12 months. In the event we are assessed interest or penalties at some point in the future, they will be classified in the consolidated financial statements as a component of income tax expense. We have not incurred any interest or penalties.

We operate in multiple jurisdictions, both within and outside the United States, and may be subject to audits from various tax authorities. Management's judgment is required in determining our provision for income taxes, our deferred tax assets and liabilities, liabilities for uncertain tax positions, and any valuation allowance recorded against our net deferred tax assets. We will monitor the extent to which our deferred tax assets may be realized and adjust the valuation allowance accordingly.

Recently Adopted Accounting Pronouncements

Refer to Note 2, "Summary of Significant Accounting Policies," in the accompanying notes to our consolidated financial statements for the years ended December 31, 2022 and 2021 for a discussion of recent accounting pronouncements.

Contractual Obligations

We enter into contracts in the normal course of business with third-party service providers for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. We have not included our payment obligations under these contracts in the table, as these contracts generally provide for termination upon notice, and therefore, we believe that our non-cancelable obligations under these agreements are not material and we cannot reasonably estimate the timing of if and when they will occur. We could also enter into additional research, manufacturing, supplier and other agreements in the future, which may require up-front payments and even long-term commitments of cash.

Emerging Growth Company and Smaller Reporting Company Status

As an EGC under the JOBS Act, we may delay the adoption of certain accounting standards until such time as those standards apply to private companies. Other exemptions and reduced reporting requirements under the JOBS Act for EGCs include presentation of only two years of audited consolidated financial statements in a registration statement for an IPO, an exemption from the requirement to provide an auditor's report on internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act, an exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation, and less extensive disclosure about our executive compensation arrangements.

In addition, the JOBS Act provides that an EGC can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an EGC to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We may remain classified as an EGC until the end of the fiscal year following the fifth anniversary of the completion of our IPO, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30 of any year before that time, or if we have annual gross revenues of $1.235 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1.0 billion of non-convertible debt over a three-year period.

We are also a "smaller reporting company," meaning that the market value of our shares held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) if the market value of our shares held by non-affiliates is more than $250 million but less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company as defined by Item 10 of Regulation S-K and are not required to provide the information otherwise required under this item.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, Exhibits and Financial Statement Schedules, of this Annual Report on Form 10-K.

Our independent public accounting firm is EY Godkendt Revisionspartnerselskab, Copenhagen, Denmark, PCAOB Auditor ID 1757.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2022.

The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under 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 are recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial and accounting officer, 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 our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Inherent Limitations of Internal Controls

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate. Our internal control over financial reporting is a process designed under the supervision of our principal executive officer and principal financial officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles.

Under the supervision and with the participation of management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control –Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on our evaluation under that framework, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act during our most recently completed fiscal quarter that has materially affected, or is 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 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference. All financial statements;

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto. Those financial statement schedules required to be filed by Item 8 of this form, and by paragraph (b) below.

(3) Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/Reg. Number
3.1	Amended and Restated Certificate of Incorporation of Registrant.	Form 8-K (Exhibit 3.1)	November 4, 2020	001-39655
3.2	Amended and Restated Bylaws of the Registrant.	Form 8-K (Exhibit 3.2)	November 4, 2020	001-39655
4.1	Specimen Common Stock Certificate.	Form S-1/A (Exhibit 4.1)	October 22, 2020	333-249369
4.2	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated September 25, 2020.	Form S-1/A (Exhibit 4.2)	October 22, 2020	333-249369
4.3*	Description of Capital Stock.			
10.1#	2020 Stock Option and Grant Plan.	Form S-1/A (Exhibit 10.1)	October 22, 2020	333-249369
10.2#	2020 Equity Incentive Plan, and forms of award agreements thereunder.	Form 10-K (Exhibit 10.2)	March 29, 2021	001-39655
10.3#	Senior Executive Cash Incentive Bonus Plan.	Form S-1/A (Exhibit 10.3)	October 22, 2020	333-249369
10.4#	Executive Separation Benefits Plan.	Form 8-K (Exhibit 10.1)	July 6, 2021	001-39655
10.5#	Form of Officer Indemnification Agreement between the Registrant and each of its executive officers.	Form S-1/A (Exhibit 10.4)	October 22, 2020	333-249369
10.6#	Form of Director Indemnification Agreement between the Registrant and each of its directors.	Form S-1/A (Exhibit 10.5)	October 22, 2020	333-249369
10.7#	Non-Employee Director Compensation Policy, as amended.	Form 8-K (Exhibit 10.1)	February 9, 2022	001-39655
10.8#	Service Agreement between Galecto Biotech ApS and Hans Schambye, dated April 23, 2013.	Form S-1/A (Exhibit 10.7)	October 22, 2020	333-249369
10.9#	Employment Contract between Galecto Biotech ApS and Anders H. Pedersen, dated January 23, 2013, as amended on August 24, 2017.	Form S-1/A (Exhibit 10.8)	October 22, 2020	333-249369
10.10#	Addendum to Employment Contract between Galecto Biotech ApS and Anders H. Pedersen, dated August 24, 2017.	Form S-1/A (Exhibit 10.9)	October 22, 2020	333-249369
10.11#	Employment Contract between Galecto Biotech ApS and Bertil E. Lindmark, dated November 28, 2019.	Form S-1/A (Exhibit 10.10)	October 22, 2020	333-249369

Exhibit Number	Exhibit Description	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.12#	Addendum to Employment Contract between Galecto Biotech ApS and Bertil E. Lindmark, dated January 15, 2020.	Form S-1/A (Exhibit 10.11)	October 22, 2020	333-249369
10.13#	Employment Agreement between Galecto, Inc. and Jonathan Freve, dated March 11, 2020.	Form S-1/A (Exhibit 10.12)	October 22, 2020	333-249369
10.14#	Amendment to Employment Agreement between Galecto, Inc. and Jonathan Freve, dated March 14, 2020.	Form S-1/A (Exhibit 10.13)	October 22, 2020	333-249369
10.15#	English language summary of Lease Agreement between Galecto Biotech ApS and COBIS A/S, dated April 5, 2021.	Form 10-Q (Exhibit 10.1)	August 5, 2021	001-39655
21.1*	List of Subsidiaries of the Registrant.			
23.1*	Consent of EY Godkendt Revisionspartnerselskab, independent registered public accounting firm.			
24.1*	Power of Attorney (included on signature page to this Annual Report on Form 10-K).			
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.			
101.INS	Inline XBRL Instance 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 (embedded within the Inline XBRL document)			

* Filed herewith.

** Furnished herewith.

# Indicates management contract or any compensatory plan, contract or arrangement.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

Galecto, Inc.

Date: March 9, 2023

By: /s/ Hans T. Schambye
Hans T. Schambye, M.D., Ph.D.
Chief Executive Officer and President

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Hans T. Schambye and Jonathan Freve, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Hans T. Schambye Hans T. Schambye, M.D., Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 9, 2023
/s/ Jonathan Freve Jonathan Freve	Chief Financial Officer (Principal Financial and Accounting Officer)	March 9, 2023
/s/ Carl Goldfischer Carl Goldfischer, M.D.	Chairman	March 9, 2023
/s/ Jayson Dallas Jayson Dallas, M.D.	Director	March 9, 2023
/s/ Chau Q. Khuong Chau Q. Khuong	Director	March 9, 2023
/s/ Søren Møller Søren Møller, Ph.D.	Director	March 9, 2023
/s/ Amit D. Munshi Amit D. Munshi	Director	March 9, 2023
/s/ Anne Prener Anne Prener, M.D., Ph.D.	Director	March 9, 2023
/s/ David Shapiro David Shapiro, M.D.	Director	March 9, 2023

GALECTO, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Galecto, Inc.

Opinion on the Financial Statements

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

Basis for Opinion

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

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

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

/s/ EY Godkendt Revisionspartnerselskab

We have served as the Company's auditor since 2019.

Copenhagen, Denmark
March 9, 2023

GALECTO, INC.

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31,	
	2022	2021
Assets		
Current assets		
Cash and cash equivalents	$ 32,786	$ 62,563
Marketable securities	27,438	37,628
Prepaid expenses and other current assets	3,686	9,911
Total current assets	63,910	110,102
Marketable securities, non-current	5,832	9,048
Operating lease right-of-use asset	810	834
Equipment, net	357	203
Other assets, non-current	2,279	2,028
Total assets	$ 73,188	$ 122,215
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	$ 3,350	$ 1,531
Accrued expenses and other current liabilities	7,757	3,013
Total current liabilities	11,107	4,544
Operating lease liabilities, non-current	328	448
Total liabilities	11,435	4,992
Commitments and contingencies (Note 9)		
Stockholders' equity		
Preferred stock, par value of $0.00001 per share; 10,000,000 shares authorized at December 31, 2022 and 2021; no shares issued or outstanding as of December 31, 2022 and 2021	—	—
Common stock, par value of $0.00001 per share; 300,000,000 shares authorized at December 31, 2022 and 2021; 25,652,392 and 25,261,832 shares issued and outstanding at December 31, 2022 and 2021, respectively	—	—
Additional paid-in capital	279,733	273,655
Accumulated deficit	(217,736)	(156,112)
Accumulated other comprehensive loss	(244)	(320)
Total stockholders' equity	61,753	117,223
Total liabilities and stockholders' equity	$ 73,188	$ 122,215

See accompanying notes to the consolidated financial statements.

GALECTO, INC.

Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2022	2021
Operating expenses		
Research and development	$ 48,206	$ 38,488
General and administrative	13,001	13,739
Total operating expenses	61,207	52,227
Loss from operations	(61,207)	(52,227)
Other income (expense), net		
Interest income, net	722	156
Loss on sale of marketable securities	(70)	—
Foreign exchange transaction gain (loss), net	(1,069)	319
Total other income (expense), net	(417)	475
Net loss	(61,624)	(51,752)
Net loss per common share, basic and diluted	$ (2.43)	$ (2.05)
Weighted-average number of shares used in computing net loss per common share, basic and diluted	25,409,123	25,261,832
Other comprehensive gain (loss), net of tax		
Currency translation gain (loss)	$ 265	$ (917)
Unrealized loss on marketable securities	(259)	(77)
Reclassification adjustment for loss included in net income	70	—
Other comprehensive gain (loss), net of tax	76	(994)
Total comprehensive loss	$ (61,548)	$ (52,746)

See accompanying notes to the consolidated financial statements.

GALECTO, INC.

Consolidated Statements of Changes in Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2020	25,261,832	$ —	$ 269,175	$ (104,360)	$ 674	$ 165,489
Stock-based compensation expense	—	—	4,480	—	—	4,480
Other comprehensive loss, net	—	—	—	—	(994)	(994)
Net loss	—	—	—	(51,752)	—	(51,752)
Balance at December 31, 2021	25,261,832	—	273,655	(156,112)	(320)	117,223
Stock-based compensation expense	—	—	5,571	—	—	5,571
Issuance of common stock; net of issuance costs of $0.2 million	390,560	—	507	—	—	507
Other comprehensive gain, net	—	—	—	—	76	76
Net loss	—	—	—	(61,624)	—	(61,624)
Balance at December 31, 2022	25,652,392	$ —	$ 279,733	$ (217,736)	$ (244)	$ 61,753

See accompanying notes to the consolidated financial statements.

GALECTO, INC.

Consolidated Statements of Cash Flows

(in thousands)

	Year Ended December 31,	
	2022	2021
Cash flows from operating activities		
Net loss	$ (61,624)	$ (51,752)
Adjustment to reconcile net loss to net cash used in operating activities:		
Depreciation of equipment	42	20
Stock-based compensation	5,571	4,480
Amortization of premiums and discounts on marketable securities	566	1,072
Net loss on sale of marketable securities	70	—
Amortization of right of use lease asset	448	421
Accretion of lease liability	58	75
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	6,232	(4,199)
Other assets, non-current	(257)	(866)
Accounts payable	1,819	(1,320)
Accrued expenses and other current liabilities	4,666	274
Operating lease liabilities	(523)	(513)
Net cash used in operating activities	(42,932)	(52,308)
Cash flows from investing activities		
Purchases of marketable securities	(44,865)	(84,209)
Proceeds from sale of marketable securities	57,445	36,384
Purchases of property and equipment	(196)	(223)
Net cash provided by (used in) investing activities	12,384	(48,048)
Cash flows from financing activities		
Proceeds from issuance of common stock, net of issuance costs	507	—
Net cash provided by financing activities	507	—
Net decrease in cash and cash equivalents	(30,041)	(100,356)
Effect of exchange rate changes on cash and cash equivalents	264	(917)
Cash and cash equivalents, beginning of year	62,563	163,836
Cash and cash equivalents, end of year	$ 32,786	$ 62,563
Supplemental disclosures of cash flow information:		
Cash paid for taxes	$ —	$ —
Supplemental disclosures of noncash activities:		
Operating lease liability arising from obtaining right-of-use assets	$ 488	$ 411

See accompanying notes to the consolidated financial statements.

1. DESCRIPTION OF BUSINESS, ORGANIZATION AND LIQUIDITY

Business

Galecto, Inc., together with its consolidated subsidiaries (the "Company" or "Galecto"), is a clinical-stage biotechnology company developing novel therapeutics that are designed to target the biological processes that lie at the heart of fibrotic diseases and cancer. The Company's initial focus is on the development of small molecule inhibitors of galectin-3 and lysyl oxidase-like 2 ("LOXL2"), which play key roles in regulating fibrosis and cancer.

As of December 31, 2022, the Company's wholly owned subsidiaries were PharmAkea, Inc. or PharmAkea, Galecto Securities Corporation and Galecto Biotech AB, a Swedish company. Galecto Biotech ApS, a Danish operating company, is a wholly-owned subsidiary of Galecto Biotech AB.

Risks and uncertainties

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance reporting capabilities.

The Company's product candidates are in development. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees and consultants.

Liquidity and management plans

Since inception, the Company has devoted substantially all its efforts to business planning, research and development, recruiting management and technical staff and raising capital, and has financed its operations primarily through the issuance of redeemable convertible preferred shares, debt financings and, most recently, the Company's initial public offering, or IPO.

As of December 31, 2022, the Company had an accumulated deficit of $217.7 million, from recurring losses since inception in 2011. The Company has incurred recurring losses and has not generated revenue as no products have obtained the necessary regulatory approval in order to market products. The Company expects to continue to incur losses as a result of costs and expenses related to the Company's clinical development and corporate general and administrative activities. The Company had negative cash flows from operating activities during the years ended December 31, 2022 and 2021 of $42.9 million and $52.3 million, respectively, and current projections indicate that the Company will have continued negative cash flows for the foreseeable future as it continues to develop its product candidates. Net losses incurred for the years ended December 31, 2022 and 2021 amounted to $61.6 million and $51.8 million, respectively.

At December 31, 2022, the Company's cash, cash equivalents and marketable securities amounted to $66.1 million, current assets amounted to $63.9 million and current liabilities amounted to $11.1 million. At December 31, 2021, the Company's cash, cash equivalents and marketable securities amounted to $109.2 million, current assets amounted to $110.1 million and current liabilities amounted to $4.5 million.

In the future, the Company will consider the following ways to fund its operations including: (1) raising additional capital through equity and/or debt financings; (2) new commercial relationships to help fund future clinical trial costs (i.e. licensing and partnerships); (3) reducing spending on one or more research and development programs by discontinuing development; and/or (4) restructuring operations to change its overhead structure. Volatility in equity capital markets may adversely affect the market price of the Company's shares of common stock, which may materially and adversely affect the Company's ability to fund its business through

public or private sales of equity securities. The Company's future liquidity needs, and ability to address those needs, will largely be determined by the success of its product candidates, key developments and regulatory events.

Coronavirus pandemic

The novel coronavirus ("COVID-19") and its variants, and ensuing pandemic, has continued to spread worldwide, causing many governments to implement measures to slow the spread of the outbreak. COVID-19 and its variants have had a significant impact, both directly and indirectly, 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 has fallen. The Company continues to monitor the impact of COVID-19 and its subvariants and assess its strategy accordingly. However, there can be no assurance that the Company will not experience additional negative impacts associated with the COVID-19 pandemic, which could decrease or delay enrollment of patients in the Company's clinical trials or otherwise cause interruptions or delays in the Company's clinical trials, programs and services, and negatively impact the Company's business, financial condition and results of operations.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of presentation

The accompanying consolidated financial statements have been prepared in conformity with United States, or U.S., generally accepted accounting principles, or GAAP. Any reference in these notes to applicable guidance is meant to refer to U.S. GAAP, as found in the Accounting Standards Codification, or ASC, and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB.

Principles of consolidation

The Company's consolidated financial statements for 2022 and 2021 include Galecto, Inc. and its subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting periods. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Significant items subject to such estimates and assumptions include contract research accruals, accounting for stock-based compensation and valuation of the Company's deferred tax assets. Changes in estimates are recorded in the period in which they become known. The Company's actual results could differ from those estimates.

Currency and currency translation

The consolidated financial statements are presented in U.S. dollars, the Company's reporting currency. Galecto, Inc., Galecto Securities Corporation and PharmAkea's functional currency is the U.S. dollar. The functional currency of the Company's subsidiary Galecto Biotech AB, and its subsidiary Galecto Biotech ApS, is the Euro. Adjustments that arise from exchange rate changes on transactions of each group entity denominated in a currency other than the functional currency are included in other income and expense in the consolidated statements of operations. Assets and liabilities of Galecto Biotech AB and Galecto Biotech ApS recorded in their Euro functional currency are translated into the U.S. dollar reporting currency of the Company at the exchange rate on the balance sheet date. Revenue and expenses of Galecto Biotech AB and Galecto Biotech ApS recorded in their Euro functional currency are translated into the U.S. dollar reporting currency of the Company at the average exchange rate prevailing during the year. Resulting translation adjustments are recorded to accumulated other comprehensive income (loss), or OCI.

Cash and cash equivalents

The Company considers all highly liquid investments with original maturities at the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents are stated at fair value and may include money market funds, U.S. Treasury and U.S. government-sponsored agency securities, corporate debt, commercial paper and certificates of deposit. The Company had money market funds of $16.4 and $49.6 million as of December 31, 2022 and 2021, respectively, which are included in cash and cash equivalents and reported at fair value (Note 4).

Concentrations of credit risk and off-balance sheet risk

Financial instruments that subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. Substantially all of the Company's cash is held at financial institutions that management believes to be of high-credit quality. The Company maintains its cash in bank deposit and checking accounts that at times exceed insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to any significant credit risk.

Investments in marketable securities

The Company invests excess cash balances in short-term and long-term marketable debt securities. The Company classifies investments in marketable debt securities as either held-to-maturity or available-for-sale based on the facts and circumstances present at the time of purchase and re-evaluates classification at each balance sheet date. All investments in marketable debt securities at each balance sheet date presented, are generally considered as available-for-sale. Marketable debt securities with maturities of twelve months or less are classified as short-term investments and marketable debt securities with maturities greater than twelve months are classified based on their availability for use in current operations.

The Company reports available-for-sale debt securities at fair value at each balance sheet date and includes any unrealized holding gains and losses (the adjustment to fair value), net of applicable taxes, in accumulated other comprehensive income (loss), a component of stockholders' equity. The cost of debt securities is adjusted for the amortization of premium and accretion of discounts to maturity. Such amortization and accretion is included in interest income. Realized gains and losses are determined using the specific identification method and are included in other income (expense). If any adjustment to fair value reflects a decline in the value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other than temporary," including the intention to sell and, if so, marks the investment to market through a charge to the Company's consolidated statements of operations and comprehensive loss.

Fair value of financial instruments

Fair value is defined as the price the Company would receive to sell an investment in a timely transaction or pay to transfer a liability in a timely transaction with an independent buyer in the principal market, or in the absence of a principal market, the most advantageous market for the investment or liability. A framework is used for measuring fair value utilizing a three-tier hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy 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).

The three levels of the fair value hierarchy are as follows:

Level 1—Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;

Level 2—Quoted prices in markets that are not considered to be active or financial instrument valuations for which all significant inputs are observable, either directly or indirectly; and

Level 3—Prices or valuations that require inputs that are both significant to the fair value measurement and unobservable.

Financial instruments are categorized in their entirety based on the lowest level of input that is significant to the fair value measurement. The assessment of the significance of a particular input to the fair value measurement requires judgment and considers factors specific to the investment. To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by us in determining fair value is greatest for instruments categorized in Level 3.

The Company monitors the availability of inputs that are significant to the measurement of fair value to assess the appropriate categorization of financial instruments within the fair value hierarchy. Changes in economic conditions or model-based valuation techniques may require the transfer of financial instruments from one fair value level to another. In such instances, our policy is to recognize significant transfers between levels at the end of the reporting period. The significance of transfers between levels is evaluated based upon the nature of the financial instrument and size of the transfer relative to total net assets available for benefits.

Leases

The Company determines whether an arrangement is or contains a lease at the time it enters into a contract. For all leases, the Company determines the classification as either operating leases or finance leases. Operating leases are included in operating lease right-of-use, or ROU, assets and accrued expenses and other current liabilities and operating lease liabilities, noncurrent in the Company's consolidated balance sheets. The Company has not entered into any financing leases.

Lease recognition occurs at the commencement date and lease liability amounts are based on the present value of lease payments over the lease term. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. If a lease does not provide information to determine an implicit interest rate, the Company uses the Company's incremental borrowing rate in determining the present value of lease payments. ROU assets represent the right to use an underlying asset for the lease term, and lease liabilities represent the obligation to make lease payments under the lease. ROU assets also include any lease payments made prior to the commencement date and exclude lease incentives received. Operating lease expense is recognized on a straight-line basis over the lease term. The depreciable life of assets and leasehold improvements are limited by the expected lease term, unless there is a transfer of title or purchase option reasonably certain of exercise. Lease agreements with both lease and non-lease components, are generally accounted for together as a single lease component. Refer to Note 6 for further details.

Property and equipment, net

Property and equipment are recorded at cost. Costs associated with maintenance and repairs are expensed as incurred. Depreciation is provided using the straight-line method over the estimated useful lives:

Asset Category	Useful Life
Equipment	5-7 years
Furniture and fixtures	5 years
Leasehold improvements	Lesser of 10 years or the remaining term of the respective lease

Impairment of long-lived assets

Long-lived assets to be held and used are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If the undiscounted cash flows are insufficient to recover the carrying value, an impairment loss is recorded for the difference between the carrying value and fair value of the asset. Through December 31, 2022, no such impairment has occurred.

Research and development expenses

Research and development costs are expensed as incurred. The Company's research and development expenses consist primarily of costs incurred for the development of its product candidates and include expenses incurred under agreements with contract manufacturing organizations, or CMOs, contract research organizations, or CROs, investigative sites and consultants to conduct clinical trials and preclinical and non-clinical studies, costs to acquire, develop and manufacture supplies for clinical trials and other studies, salaries and related costs, including stock-based compensation, depreciation and other allocated facility-related and overhead expenses and licensing fees and milestone payments incurred under product license agreements where no alternative future use exists.

The Company has met the requirements to receive a tax credit in Denmark for losses resulting from research and development costs of up to $3.6 million and $3.8 million for the years ended December 31, 2022 and 2021, respectively. The tax credit is reported as a reduction to research and development expense in the consolidated statements of operations. For the years ended December 31, 2022 and 2021, research and development expenses include refundable tax credits of $0.8 million and $0.9 million, respectively.

Accrued research and development costs

Substantial portions of the Company's preclinical and clinical trials are performed by third-party laboratories, medical centers, CROs and other vendors, or collectively, CROs. These CROs generally bill monthly for services performed, or bill based upon milestone achievement. For preclinical studies, the Company accrues expenses based upon estimated percentage of work completed and the contract milestones remaining. For clinical studies, expenses are accrued based upon the number of patients enrolled and the duration of the study. The Company monitors patient enrollment, the progress of clinical studies and related activities to the extent possible through internal reviews of data reported to the Company by the CROs, and correspondence with the CROs and clinical site visits.

The Company's estimates depend on the timeliness and accuracy of the data provided by the CROs regarding the status of each program and total program spending. The Company periodically evaluates the estimates to determine if adjustments are necessary or appropriate based on information it receives.

Stock-based compensation

The Company accounts for stock options granted in accordance with ASC 718, *Compensation-Stock Compensation*, or ASC 718. In accordance with ASC 718, compensation expense is measured at the estimated fair value of the stock options at grant date and is included as compensation expense over the vesting period during which an employee provides service in exchange for the award.

All share-based awards granted are measured based on the fair value on the date of the grant and compensation expense is recognized with respect to those awards over the requisite service period, which is generally the vesting period of the respective award. The Company reverses any previously recognized compensation cost associated with forfeited awards in the period the forfeiture occurs.

Equity-based compensation expense is classified in the Company's consolidated statement of operations and comprehensive loss in the same manner in which the award recipients' payroll costs are classified or in which the award recipients' service payments are classified. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes model. The following summarizes the inputs used:

Expected volatility—The Company estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies because we lack company-specific historical and implied volatility information due in part to the limited time in which we have operated as a publicly traded company. We expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price.

Expected term—The expected term of the Company's stock options has been determined based on the expected time to liquidity. The Company uses the simplified method prescribed by the SEC's Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term of options granted because we lack company-specific historical and implied expected term information due in part to the limited time in which we have operated as a publicly traded company.

Risk-free interest rate—The risk-free interest rate is based on the implied yield on a U.S. Treasury security at a constant maturity with a remaining term equal to the expected term of the option granted.

Dividends—Expected dividend yield is zero because the Company does not pay cash dividends on common shares and does not expect to pay any cash dividends in the foreseeable future.

Income taxes

Deferred income tax assets and liabilities arise from temporary differences associated with differences between the financial statements and tax basis of assets and liabilities, as measured by the enacted tax rates, which are expected to be in effect when these differences reverse. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized.

The Company has generated net losses since inception and accordingly has not recorded a provision for income taxes.

The Company follows the provisions of ASC 740-10, *Uncertainty in Income Taxes,* or ASC 740-10. The Company has not recognized a liability as a result of the implementation of ASC 740-10. A reconciliation of the beginning and ending amount of unrecognized tax benefits has not been provided since there is no unrecognized benefit since the date of adoption. The Company has not recognized interest expense or penalties as a result of the implementation of ASC 740-10. If there were an unrecognized tax benefit, the Company would recognize interest accrued related to unrecognized tax benefits and penalties in income tax expense.

The Company has identified the United States, Denmark and United Kingdom as its major tax jurisdictions. Refer to Note 11 for further details.

Net loss per share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock outstanding for the period. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock and dilutive common stock equivalents outstanding for the period, determined using the treasury-stock method and the as if-converted method, for convertible securities, if inclusion of these instruments is dilutive.

For the years ended December 31, 2022 and 2021, both methods are equivalent. Basic and diluted net loss per share is described further in Note 12.

Segments

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the chief operating decision maker, or CODM, in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its chief executive officer. The Company has determined it operates in one segment.

Other comprehensive gain (loss)

Other comprehensive gain (loss), or OCI, is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The Company's OCI includes currency translation and unrealized gain or (loss) on marketable securities.

Emerging growth company status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act, until such time as those standards apply to private companies. The Company may elect to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, and as a smaller reporting company, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently adopted accounting standards

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments-Credit Losses: Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 requires measurement and recognition of expected credit losses for financial assets. In April 2019, the FASB issued clarification to ASU 2016-13 within ASU 2019-04, *Codification Improvements to Topic 326, Financial Instruments-Credit Losses, Topic 815, Derivatives and Hedging*, *and Topic 825, Financial Instruments*. The ASU 2016-13 guidance became effective as of January 1, 2020, and must be adopted using a modified retrospective approach, with certain exceptions. This guidance is effective for public business entities that meet the definition of a SEC, excluding eligible smaller reporting companies for fiscal years beginning after December 15, 2019. For all other entities, including emerging growth companies, it is effective for fiscal years beginning after December 15, 2022. The adoption of ASU No. 2016-13 during the year ended December 31, 2022 did not have a material impact on the financial statements.

Recently issued accounting standards

The Company periodically reviews new accounting standards that are issued and has not identified any new standards that it believes merit further discussion or would have a significant impact on its financial statements.

3. INVESTMENTS IN MARKETABLE SECURITIES

Cash in excess of the Company's immediate requirements is invested in accordance with the Company's investment policy that primarily seeks to maintain adequate liquidity and preserve capital.

A summary of the Company's available-for-sale investments as of December 31, 2022 and 2021 consisted of the following (in thousands):

	At December 31, 2022			
Marketable securities:	**Amortized Cost**	**Gross Unrealized Gains**	**Gross Unrealized Losses**	**Fair Value**
Corporate bonds	$ 27,573	$ —	$ (135)	$ 27,438
Total	$ 27,573	$ —	$ (135)	$ 27,438
Marketable securities, non-current:				
Corporate bonds	$ 5,963	$ —	$ (131)	$ 5,832
Total	$ 5,963	$ —	$ (131)	$ 5,832

	At December 31, 2021			
Marketable securities:	**Amortized Cost**	**Gross Unrealized Gains**	**Gross Unrealized Losses**	**Fair Value**
Corporate bonds	$ 37,671	$ —	$ (43)	$ 37,628
Total	$ 37,671	$ —	$ (43)	$ 37,628
Marketable securities, non-current:				
Corporate bonds	$ 9,082	$ —	$ (34)	$ 9,048
Total	$ 9,082	$ —	$ (34)	$ 9,048

4. FAIR VALUE MEASUREMENTS

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value are performed in a manner to maximize the use of observable inputs and minimize the use of unobservable inputs.

The Company classified its money market funds within Level 1 because their fair values are based on their quoted market prices. The Company classified its debt securities within Level 2 because their fair values are determined using alternative pricing sources or models that utilized market observable inputs.

A summary of the assets that are measured at fair value as of December 31, 2022 and 2021 is as follows (in thousands):

	Fair Value Measurement at December 31, 2022			
Assets:	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds[1]	$ 16,445	$ 16,445	$ —	$ —
Debt securities	33,270	—	33,270	—
Total	$ 49,715	$ 16,445	$ 33,270	$ —

	Fair Value Measurement at December 31, 2021			
Assets:	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds[1]	$ 49,626	$ 49,626	$ —	$ —
Debt securities	46,676	—	46,676	—
Total	$ 96,302	$ 49,626	$ 46,676	$ —

(1) Money market funds with maturities of 90 days or less at the date of purchase are included within cash and cash equivalents in the accompanying consolidated balance sheets and are recognized at fair value.

5. PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets consist of the following (in thousands):

	December 31,	
	2022	2021
Contract research and development costs	$ 1,450	$ 5,569
Prepaid insurance costs	805	1,728
Research and development tax credit receivable	792	1,682
Value-added tax refund receivable	587	598
Other	52	334
Total prepaid expenses and other current assets	$ 3,686	$ 9,911

6. LEASES

The Company has the following operating leases:

Location	Primary Use	Lease Expiration Date	Renewal Option
Copenhagen, Denmark	Corporate headquarters	January 2025	None
London, United Kingdom	Office space	February 2024	None
Gothenburg, Sweden	Office space	May 2023	None
Stevenage, United Kingdom	Laboratory space	August 2025	None

The Company has no finance leases and has elected to apply the short-term lease exception to all leases of one year or less. Rent expense for years ended December 31, 2022 and 2021 was $0.5 million for both periods.

Quantitative information regarding the Company's leases for the years ended December 31, 2022 and 2021 is as follows (in thousands):

	Year Ended December 31,	
Lease Cost:	**2022**	**2021**
Operating lease cost	$ 506	$ 496
Other Information:		
Operating cash flows paid for amounts included in the measurement of lease liabilities	$ 523	$ 513
Operating lease liabilities arising from obtaining right-of-use assets	$ 488	$ 411

As of December 31, 2022 and 2021, the weighted average remaining lease term for operating leases was 1.8 years and 2.4 years, respectively.

As of December 31, 2022 and 2021, the weighted average discount rate for operating leases was 8% for both periods.

Operating lease liabilities are as follows at December 31, 2022 (in thousands):

	Operating Leases
2023	$ 523
2024	293
2025	51
2026	—
2027	—
Total lease payments	867
Less: imputed interest	(63)
Total lease liabilities	$ 804

7. PROPERTY AND EQUIPMENT, NET

Equipment as of December 31, 2022 and 2021 consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Equipment	$ 419	$ 223
Less: accumulated depreciation	(62)	(20)
Equipment, net	$ 357	$ 203

Depreciation expense for the years ended December 31, 2022 and 2021 was $42,000 and $20,000, respectively.

8. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consist of the following (in thousands):

	December 31,	
	2022	2021
Contract research and development costs	$ 6,145	$ 1,575
Employee compensation costs	597	601
Lease liabilities, current	476	399
Other current liabilities	539	438
Total accrued expenses and other current liabilities	$ 7,757	$ 3,013

9. COMMITMENTS AND CONTINGENCIES

Lease commitments

The Company's commitments related to lease agreements are disclosed in Note 6.

Legal proceedings

From time to time, the Company may be party to litigation arising in the ordinary course of its business. The Company was not subject to any material legal proceedings during the years ended December 31, 2022 and 2021, and, to its knowledge, no material legal proceedings are currently pending or threatened.

Indemnification agreements

The Company, as permitted under Delaware law and in accordance with its certification of incorporation and bylaws and pursuant to indemnification agreements with certain of its officers and directors, indemnifies its officers and directors for certain events or occurrences, subject to certain limits, which the officer or director is or was serving at the Company's request in such capacity.

The Company enters into certain types of contracts that contingently requires the Company to indemnify various parties against claims from third parties. These contracts primarily relate to (i) the Company's bylaws, under which the Company must indemnify directors and executive officers, and may indemnify other officers and employees, for liabilities arising out of their relationship, (ii) contracts under which the Company must indemnify directors and certain officers and consultants for liabilities arising out of their relationship, and (iii) procurement, service or license agreements under which the Company may be required to indemnify vendors, service providers or licensees for certain claims, including claims that may be brought against them arising from the Company's acts or omissions with respect to the Company's products, technology, intellectual property or services.

From time to time, the Company may receive indemnification claims under these contracts in the normal course of business. In the event that one or more of these matters were to result in a claim against the Company, an adverse outcome, including a judgment or settlement, may cause a material adverse effect on the Company's future business, operating results or financial condition. It is not possible to estimate the maximum amount potentially payable under these contracts since the Company has no history of prior indemnification claims and the unique facts and circumstances involved in each particular claim will be determinative.

10. STOCK-BASED COMPENSATION

Employee equity plan

In March 2020, the Company's Board of Directors and stockholders approved the 2020 Stock Option and Grant Plan ("2020 Plan"). Holders of stock options under the 2020 Plan shall be entitled to exercise the vested portion of the stock option during the term of the grant. If a qualified exit, as defined in the 2020 Plan, occurs, then all of the holders' unvested options shall vest immediately.

In October 2020, the Company's Board of Directors and stockholders approved the 2020 Equity Incentive Plan ("2020 Equity Plan"). Following the adoption of the 2020 Equity Plan, no further options are available to be issued under the 2020 Plan. Stock options granted under the 2020 Equity Plan generally vest over a four-year period and expire ten years from the grant date. The 2020 Equity Plan will cumulatively increase by 5 percent of the number of shares of common stock issued and outstanding on January 1st each year until 2030. At December 31, 2022, the Company had 884,566 options available for future grant under the 2020 Equity Plan.

The following table sets forth the activity for the Company's stock options during the periods presented:

	Number of Options	Weighted-average exercise price per share	Weighted-average remaining contractual term (in years)	Aggregate intrinsic value
Outstanding at December 31, 2020	2,538,411	$ 4.67	8.8	20,009,769
Granted	1,631,000	9.49	—	8,160
Cancelled	(170,683)	7.63	—	—
Outstanding at December 31, 2021	3,998,728	6.51	8.3	$ 1,357,655
Granted	1,827,750	2.98	—	111,013
Cancelled	(47,593)	2.73	—	—
Outstanding at December 31, 2022	5,778,885	$ 5.43	7.9	$ —
Vested and expected to vest at December 31, 2022	5,474,743	$ 5.43	8.3	$ —
Vested and exercisable at December 31, 2022	2,667,144	$ 5.65	7.1	$ —

The weighted-average grant date fair value of all stock options granted during the year ended December 31, 2022 was $2.22. The intrinsic value at December 31, 2022 and 2021 is based on the closing price of the Company's common stock on that date of $1.15 and $3.03 per share, respectively.

Stock-based compensation

The grant date fair value of stock options vested during the years ended December 31, 2022 and 2021 was $6.8 million and $2.6 million, respectively. Total unrecognized compensation expense related to unvested options granted under the Company's stock-based compensation plan was $10.9 million at December 31, 2022, which is expected to be recognized over a weighted average period of 2.2 years. The Company recorded stock-based compensation expense related to the issuance of stock as follows (in thousands):

	For the Year Ended December 31,	
	2022	2021
Research and development	$ 2,618	$ 1,903
General and administrative	2,953	2,577
Total Stock-based compensation	$ 5,571	$ 4,480

The Company uses a Black-Scholes option pricing model to determine fair value of its stock options. The Black-Scholes option pricing model includes various assumptions, including the fair value of common shares, expected life of stock options, the expected volatility based on the historical volatility of a publicly traded set of peer companies and the expected risk-free interest rate based on the implied yield on a U.S. Treasury security. The fair values of the options granted were estimated based on the Black-Scholes model, using the following assumptions:

	2022	2021
Risk-free interest rate	1.7%	0.7%
Expected term (in years)	6.0	6.0
Expected volatility	90.0%	90.5%
Expected dividend yield	0%	0%

11. INCOME TAXES

The Company had no income tax expense or benefit for the years ended December 31, 2022 and 2021. The Company has incurred net operating losses for all the periods presented. The Company has not reflected the benefit of any such net operating loss carryforwards in the accompanying financial statements. In 2019 the domicile of the reporting entity has changed from Denmark to the United States resulting in a tax rate of 21% in 2022 and 2021. This is discussed further below.

The components of net loss are as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Domestic	$ (10,163)	$ (11,252)
Foreign	(51,461)	(40,500)
Total	$ (61,624)	$ (51,752)

Reconciliation of effective tax rate

The effective tax rate for the years ended December 31, 2022 and 2021 is different from the statutory rate primarily due to the valuation allowance against deferred tax assets as a result of insufficient sources of income. The reconciliation of the statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2022	2021
Income tax benefit at the statutory rate	21.0%	21.0%
Orphan Drug Credit	6.6	5.7
Permanent differences	2.5	3.5
State income taxes	1.1	1.3
Foreign rate differential	0.8	0.8
Change in valuation allowance	(32.0)	(32.3)
Total	—%	—%

Deferred taxes

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The principal components of the Company's deferred tax assets and liabilities consisted of the following (in thousands):

	December 31,	
Deferred tax assets:	2022	2021
Net operating loss carryforwards	$ 43,716	$ 31,022
Orphan drug credit	8,036	3,948
U.S. research and development credits	1,191	1,191
Bonus compensation	544	274
Total deferred tax assets	$ 53,487	$ 36,435
Valuation allowance	(53,472)	(36,435)
Net deferred tax assets	15	—
Deferred tax liabilities:		
Fixed assets	(15)	—
Total deferred tax liabilities	(15)	—
Net noncurrent deferred tax asset(liability)	$ —	$ —

In assessing the realizability of deferred tax assets, management considers whether it is more-likely-than-not that some portion or all of the deferred tax assets will not be realized. The Company regularly assesses the likelihood that the deferred tax assets will be recovered from future taxable income. The Company considers projected future taxable income and ongoing tax planning strategies, then records a valuation allowance to reduce the carrying value of the net deferred taxes to an amount that is more-likely-than-not able to be realized. Based upon the Company's assessment of all available evidence, including the previous three years of taxable income and loss after permanent items, estimates of future profitability, and the Company's overall prospects of future business, the Company determined that it is more-likely-than-not that the Company will not be able to realize a portion of the deferred tax assets in the future. The Company will continue to assess the potential realization of deferred tax assets on an annual basis, or an interim basis if circumstances warrant. If the Company's actual results and updated projections vary significantly from the projections used as a basis for this determination, the Company may need to change the valuation allowance against the gross deferred tax assets. On the basis of this evaluation, a full valuation allowance at December 31, 2022 and December 31, 2021 was recorded of $53.5 million and $36.4 million, respectively, to reduce the net deferred tax assets to their estimated realizable value. The change in valuation allowance was $17.0 million.

The Company is subject to taxation in the United States, United Kingdom and Denmark. As of December 31, 2022, tax years 2019 and forward were generally open to examination by the Danish tax authorities and tax year 2021 and forward was open to examination by the United States tax authorities. The Company is not under examination by any taxing authorities.

As of December 31, 2022, the Company had gross U.S. federal net operating losses, or NOLs, of $30.7 million and federal research and development credits, or R&D credits, of $1.2 million and Orphan Drug Credit, or ODC, of $8.0 million to offset tax liabilities. The federal R&D credit and ODC carryforwards begin to expire in 2033 and 2042, respectively. All of the federal NOLs have an infinite life. The Company also had gross state NOLs of $26.8 million, which are available to offset state tax liabilities. The state NOLs begin to expire in 2040. The Company also had NOLs in Denmark of $161.7 million which have an indefinite life. Federal and state NOLs and R&D credit and ODC carryforwards are also subject to annual limitations in the event that cumulative changes in the ownership interests of significant stockholders exceed 50% over a three-year period, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986. The Company has not completed an analysis to determine if the NOLs and R&D credits are limited due to a change in ownership.

The Company recognizes accrued interest related to unrecognized tax benefits and penalties as income tax expense. The Company does not have any material unrecognized tax benefits which would affect the effective tax rate if recognized. The Company does not have any unrecognized tax benefits which would reverse within the next twelve months.

The Company is eligible for the Danish enhanced research and development tax allowance, providing for an increase in the deductible value of the amount of certain R&D expenditures. The deduction for R&D expenditures is set at 101.5% for 2019, 130% for 2020 through 2022, 108% for 2023 through 2025 and 110% for 2026.

12. NET LOSS PER SHARE

Basic and diluted net loss per share is calculated as follows (in thousands except share and per share amounts):

	Year Ended December 31,	
	2022	2021
Net loss	$ (61,624)	$ (51,752)
Weighted-average number of shares used in computing net loss per common share, basic and diluted	25,409,123	25,261,832
Net loss per common share, basic and diluted	$ (2.43)	$ (2.05)

The following outstanding potentially dilutive securities have been excluded from the calculation of diluted net loss per share, as their effect is anti-dilutive:

	Year Ended December 31,	
	2022	2021
Stock options to purchase common stock	5,778,885	3,998,728

13. DEFINED CONTRIBUTION PLAN

The Company has a 401(k)-defined contribution plan (the "401(k) Plan") for its U.S. based employees. Eligible employees may make pretax contributions to the 401(k) Plan up to statutory limits. At the discretion of its Board, the Company may elect to match employee contributions. For the years ended December 31, 2022 and 2021, the Company paid a match of up to 6%, up to the maximum permitted by the Internal Revenue Code, which amounted to $0.1 million during both periods and is expensed as personnel costs when incurred.

14. RELATED PARTY TRANSACTIONS

During the years ended December 31, 2022 and 2021, the Company had no material related party transactions.

15. SUBSEQUENT EVENTS

The Company has evaluated subsequent events through the date on which the consolidated financial statements were issued. The Company has concluded that no subsequent events have occurred that require disclosure to the consolidated financial statements.