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, 2021

OR

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

For the transition period from _____ to _____

Commission file number 001-36333

BIO-PATH HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	87-0652870
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
4710 Bellaire Boulevard, Suite 210, Bellaire, Texas	77401
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (832) 742-1357

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.001 per share	BPTH	The Nasdaq Capital Market

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

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

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

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

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

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

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

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

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

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

As of March 3, 2022, there were 7,160,164 shares of the registrant's common stock issued and outstanding. The aggregate market value of the voting stock held by non-affiliates of the registrant was approximately $46,197,553.90 as of June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, based on the last sales price of the registrant's common stock as reported on The Nasdaq Capital Market on such date. For purposes of the preceding sentence only, all directors, executive officers and beneficial owners of 10% or more of the shares of the registrant's common stock are assumed to be affiliates.

DOCUMENTS INCORPORATED BY REFERENCE: NONE

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Unless the context requires otherwise, references in this Annual Report on Form 10-K to "we," "our," "us," "the Company" and "Bio-Path" refer to Bio-Path Holdings, Inc. and its subsidiary. Bio-Path Holdings, Inc.'s wholly-owned subsidiary, Bio-Path, Inc., is sometimes referred to herein as "Bio-Path Subsidiary."

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Forward-looking statements can be identified by words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," "project," "goal," "strategy," "future," "likely," "may," "should," "will" and variations of these words and similar references to future periods, although not all forward-looking statements contain these identifying words. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent risks, uncertainties and changes in circumstances, including those discussed in "Item 1A. Risk Factors" of this Annual Report on Form 10-K and in other reports or documents we file with the U.S. Securities and Exchange Commission ("SEC"). As a result, our actual results and financial condition may differ materially from those expressed or forecasted in the forward-looking statements, and you should not rely on such forward-looking statements. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, the following:

- the impact, risks and uncertainties related to COVID-19 and actions taken by governmental authorities or others in connection therewith;
- our lack of significant revenue to date, our history of recurring operating losses and our expectation of future operating losses;
- our need for substantial additional capital and our need to delay, reduce or eliminate our drug development and commercialization efforts if we are unable to raise additional capital;
- the highly-competitive nature of the pharmaceutical and biotechnology industry and our ability to compete effectively;
- the success of our plans to use collaboration arrangements to leverage our capabilities;
- our ability to retain and attract key personnel;
- the risk of misconduct of our employees, agents, consultants and commercial partners;
- disruptions to our operations due to expansions of our operations;
- the costs we would incur if we acquire or license technologies, resources or drug candidates;
- risks associated with product liability claims;
- our reliance on information technology systems and the liability or interruption associated with cyber-attacks or other breaches of our systems;
- our ability to use net operating loss carryforwards;
- provisions in our charter documents and state law that may prevent a change in control;
- work slowdown or stoppage at government agencies could negatively impact our business;

- our need to complete extensive clinical trials and the risk that we may not be able to demonstrate the safety and efficacy of our drug candidates;
- risks that that our clinical trials may be delayed or terminated;
- our ability to obtain domestic and/or foreign regulatory approval for our drug candidates;
- changes in existing laws and regulations affecting the healthcare industry;
- our reliance on third parties to conduct clinical trials for our drug candidates;
- our ability to maintain orphan drug exclusivity for our drug candidates;
- our reliance on third parties for manufacturing our clinical drug supplies;
- risks associated with the manufacture of our drug candidates;
- our ability to establish sales and marketing capabilities relating to our drug candidates;
- market acceptance of our drug candidates;
- third-party payor reimbursement practices;
- our ability to adequately protect the intellectual property of our drug candidates;
- infringement on the intellectual property rights of third parties;
- costs and time relating to litigation regarding intellectual property rights;
- our ability to adequately prevent disclosure by our employees or others of trade secrets and other proprietary information;
- our need to raise additional capital;
- the volatility of the trading price of our common stock;
- our common stock being thinly traded;
- our ability to issue shares of common or preferred stock without approval from our stockholders;
- our ability to pay cash dividends;
- costs and expenses associated with being a public company;
- our ability to maintain effective internal controls over financial reporting; and
- our ability to maintain compliance with the listing standards of the Nasdaq Capital Market.

Please also refer to “Item 1A. Risk Factors” of this Annual Report on Form 10-K and other reports or documents we file with the SEC for a discussion of risks and factors that could cause our actual results and financial condition to differ materially from those expressed or forecasted in this Annual Report on Form 10-K.

Any forward-looking statement made by us in this Annual Report on Form 10-K is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking

statement, whether as a result of new information, future developments or otherwise. However, you should carefully review the risk factors set forth in other reports or documents we file from time to time with the SEC.

PART I

ITEM 1. BUSINESS

Overview

We are a clinical and preclinical stage oncology focused RNAi nanoparticle drug development company utilizing a novel technology that achieves systemic delivery for target specific protein inhibition for any gene product that is over-expressed in disease. Our drug delivery and antisense technology, called DNAbilize®, is a platform that uses P-ethoxy, which is a deoxyribonucleic acid (DNA) backbone modification that is intended to protect the DNA from destruction by the body's enzymes when circulating in vivo, incorporated inside of a lipid bilayer having neutral charge. We believe this combination allows for high efficiency loading of antisense DNA into non-toxic, cell-membrane-like structures for delivery of the antisense drug substance into cells. In vivo, the DNAbilize® delivered antisense drug substances are systemically distributed throughout the body to allow for reduction or elimination of target proteins in blood diseases and solid tumors. Through testing in numerous animal studies and treatment in over 80 patients, our DNAbilize® drug candidates have demonstrated an excellent safety profile. DNAbilize® is a registered trademark of the Company.

Using DNAbilize® as a platform for drug development and manufacturing, we currently have four drug candidates in development to treat at least five different cancer disease indications. Our lead drug candidate, prexigebersen (pronounced prex" i je ber' sen), which targets growth factor receptor-bound protein 2 (Grb2), initially started the efficacy portion of a Phase 2 clinical trial for untreated acute myeloid leukemia ("AML") patients in combination with low-dose cytarabine ("LDAC"). The interim data released on March 6, 2019 showed that 11 (65%) of the 17 evaluable patients had a response, including five (29%) who achieved complete remission ("CR"), including one CR with incomplete hematologic recovery ("CRi") and one morphologic leukemia free state, and six (35%) stable disease responses, including two patients who had greater than a 50% reduction in bone marrow blasts. However, DNA hypomethylating agents are now the most frequently used agents in the treatment of elderly AML patients in the U.S. and Europe. As a result, Stage 2 of the Phase 2 trial in AML was amended to remove the combination treatment of prexigebersen and LDAC and replace it with the combination treatment of prexigebersen and decitabine, a DNA hypomethylating agent, for treatment of a second cohort of untreated AML patients. Since decitabine is also used as a treatment for relapsed/refractory AML patients, a cohort of relapsed/refractory AML patients was also added to the study.

The U.S. Food and Drug Administration ("FDA") granted approval of venetoclax in combination with LDAC, decitabine or azacytidine (the latter two drugs are DNA hypomethylating agents) as frontline therapy for newly diagnosed AML in adults who are 75 years or older, or who have comorbidities precluding intensive induction chemotherapy. We believe approval of the frontline venetoclax and decitabine combination therapy provides an opportunity for combining prexigebersen with the combination therapy for the treatment of *de novo* AML patients. Preclinical efficacy studies for the triple combination treatment of prexigebersen, decitabine and venetoclax in AML have been successfully completed. In the preclinical efficacy studies, four AML cancer cell lines were treated with three different combinations of decitabine, venetoclax and prexigebersen. Decrease in AML cell viability was the primary measure of efficacy. The triple combination of decitabine, venetoclax and prexigebersen showed significant improvement in efficacy in three of the four AML cell lines. Based on these results, we believe that adding prexigebersen to the treatment combination of decitabine and venetoclax could lead to improved efficacy in AML patients. Accordingly, we further amended Stage 2 of this Phase 2 clinical trial to add the triple combination treatment comprised of prexigebersen, decitabine and venetoclax.

Bio-Path's approved amended Stage 2 for this Phase 2 clinical trial currently has three cohorts of patients. The first two cohorts will treat patients with the triple combination of prexigebersen, decitabine and venetoclax. The first cohort will include untreated AML patients, and the second cohort will include relapsed/refractory AML patients. Finally, the third cohort will treat relapsed/refractory AML patients, who are venetoclax-resistant or -intolerant, with the two-drug combination of prexigebersen and decitabine. The full trial design plans have approximately 98 evaluable patients for the first cohort having untreated AML patients with a preliminary review performed after 19 evaluable patients and a formal interim analysis after 38 evaluable patients. The full trial design plans have approximately 54 evaluable patients for each of the second cohort, having relapsed/refractory AML patients, and the third cohort, having AML patients who are venetoclax-resistant or -intolerant, in each case with a review performed after 19 evaluable patients. The study is anticipated to be conducted at ten clinical sites in the U.S., and Gail J. Roboz, M.D., is the national coordinating Principal Investigator for the Phase 2 trial. Dr. Roboz is a professor of medicine and director of the Clinical and Translational Leukemia Program at the Weill Medical College of Cornell University ("Weill Medical College") and the New York-Presbyterian Hospital in New York City. On August 13, 2020, we announced the enrollment and dosing of the first patient in this approved amended Stage 2 of the Phase 2 clinical trial.

On April 5, 2021, we announced the successful completion of the safety run-in of Stage 2 of the Phase 2 clinical study. In the safety run-in of the triple combination, six evaluable patients were treated with the combination of prexigebersen, decitabine and venetoclax. These patients included four relapsed/refractory AML patients, and two newly diagnosed AML patients. In the preliminary safety data review, five of the patients (83%) responded to treatment, including four (67%) achieving CR and one (17%) achieving CRi. Recent publications provide that CR rates to combination treatment with decitabine and venetoclax (but without prexigebersen) are 42 to 52% for relapsed/refractory AML patients and 0 to 39% for relapsed/refractory secondary AML patients. Response rates to frontline treatment with decitabine and venetoclax (but without prexigebersen) are 62 to 71% for newly diagnosed AML patients. These preliminary data, presented at the 2021 American Society of Hematology Annual Meeting, showed the treatment was well-tolerated and there were no dose limiting toxicities attributed to prexigebersen. Three patients remained on treatment for more than one cycle.

In addition, a modified product named prexigebersen-A, Bio-Path's fourth drug candidate, was shown to enhance chemotherapy efficacy in preclinical solid tumor models. Prexigebersen-A incorporates the same drug substance as prexigebersen but has a slightly modified formulation designed to enhance nanoparticle properties. In late 2019, we filed an Investigational New Drug ("IND") application to initiate a Phase 1/1b clinical trial of prexigebersen-A in patients with solid tumors, including ovarian, endometrial, pancreatic and breast cancer. Ovarian cancer is one of the most common types of gynecologic malignancies, with approximately 50% of all cases occurring in women older than 63 years. On October 27, 2021, we announced that the FDA cleared the IND application for prexigebersen-A for the initial Phase 1/1b clinical trial. The Phase 1/1b study will be conducted at leading centers, including The University of Texas MD Anderson Cancer Center ("MD Anderson Cancer Center") and The Mary Crowley Cancer Center. Shannon Westin, MD is the national coordinating Principal Investigator for the Phase 1/1b study. Dr. Westin is an associate professor in the Department of Gynecologic Oncology and Reproductive Medicine at MD Anderson Cancer Center.

Our second drug candidate, Liposomal Bcl-2 ("BP1002"), targets the protein Bcl-2, which is responsible for driving cell survival in up to 60% of all cancers. On November 21, 2019, we announced that the FDA cleared an IND application for BP1002 for an initial Phase 1 clinical trial that will evaluate the ability of BP1002 to treat refractory/relapsed lymphoma and chronic lymphocytic leukemia ("CLL") patients. The Phase 1 clinical trial is being conducted at several leading cancer centers, including MD Anderson Cancer Center and the Georgia Cancer Center. On November 19, 2020, we announced the enrollment and dosing of the first patient in the Phase 1 clinical trial.

Additionally, on August 24, 2021, we announced that the FDA cleared an IND application for BP1002 for an initial Phase 1/ 1b clinical trial that will evaluate the ability of BP1002 to treat refractory/relapsed AML patients. The Phase 1/1b clinical trial is anticipated to be conducted at several leading cancer centers in the United States, including the Weill Medical College, MD Anderson Cancer Center and the Georgia Cancer Center. Gail J. Roboz, M.D., will serve as Principal Investigator for the Phase 1/1b trial.

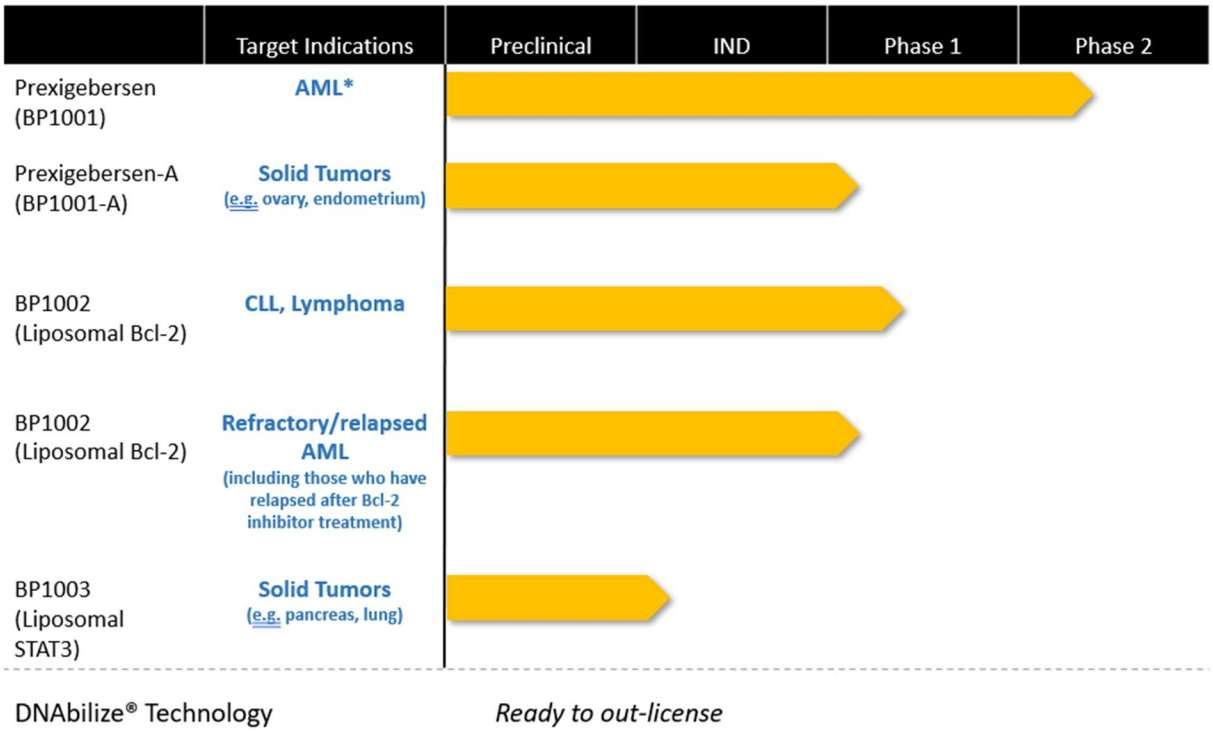
Our third drug candidate, Liposomal STAT3 ("BP1003"), targets the STAT3 protein and is currently in IND enabling studies as a potential treatment of pancreatic cancer, non-small cell lung cancer ("NSCLC") and AML. Preclinical models have shown BP1003 to inhibit cell viability and STAT3 protein expression in NSCLC and AML cell lines. Further, BP1003 successfully penetrated pancreatic tumors and significantly enhanced the efficacy of gemcitabine, a treatment for patients with advanced pancreatic cancer, in a pancreatic cancer patient derived tumor model. Our lead indication for BP1003 is pancreatic cancer due to the severity of this disease and the lack of effective, life-extending treatments. For example, pancreatic adenocarcinoma is projected to be the second most lethal cancer behind lung cancer by 2030. Typical survival for a metastatic pancreatic cancer patient is about three to six months from diagnosis. We successfully completed several IND enabling studies of BP1003 in 2021 and expect to complete one additional IND enabling study in 2022. If that additional study is successfully completed, our goal is to file an IND in 2022. Based on the filing of the IND, we expect to initiate the first-in-humans Phase 1 study of BP1003 in patients with refractory, metastatic solid tumors, including pancreatic cancer and NSCLC.

Our DNAbilize® technology-based products are available for out-licensing or partnering. We intend to apply our drug delivery technology template to new disease-causing protein targets to develop new nanoparticle antisense RNAi drug candidates. We have a new product identification template in place to define a process of scientific, preclinical, commercial and intellectual property evaluation of potential new drug candidates for inclusion into our drug product development pipeline. As we expand, we will look at indications where a systemic delivery is needed and antisense RNAi nanoparticles can be used to slow, reverse or cure a disease, either alone or in combination with another drug.

We have certain intellectual property as the basis for our current drug products in clinical development, prexigebersen, prexigebersen-A, BP1002 and BP1003. We are developing RNAi antisense nanoparticle drug candidates based on our own patented technology to treat cancer and autoimmune disorders where targeting a single protein may be advantageous and result in reduced patient adverse effects as compared to small molecule inhibitors with off-target and non-specific effects. We have composition of matter and method of use intellectual property for the design and manufacture of antisense RNAi nanoparticle drug products.

Our pipeline for development of antisense therapeutics is set forth in Figure 1 below:

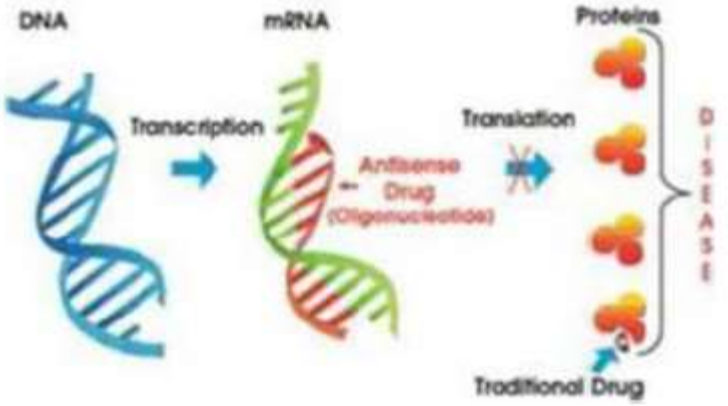
Figure 1. Bio-Path Pipeline for Development of Therapeutics



* Received orphan drug designation from the U.S. FDA and from the European Medicines Agency (EMA) for AML

Our basic drug development concept is to block expression of proteins associated with disease. Messenger RNA (mRNA) is essential in the process of creating proteins. We have developed DNAbilize® nanoparticle drug delivery systems to deliver short strands of antisense DNA drugs to cells and block the production of proteins associated with disease progression (Figure 2).

Figure 2.



Antisense DNA therapeutics is the field of designing short DNA sequences that are complementary to a mRNA for a protein of interest with the intention of inhibiting the production of the targeted protein. The DNA will find the matching RNA and form a complex. The complexed RNA will not have access to the protein-making machinery, which prevents the cell from translating it into a protein. Thus, protein production is turned off and levels of the targeted protein are reduced in the cell. This gene-specific process of controlling protein expression has led to great interest in using antisense DNA to shut off the production of proteins involved in disease. Antisense therapeutics have been in development for over 20 years. However, challenges to antisense therapeutics, such as instability of antisense drugs inside of the body and inefficient delivery of antisense to disease cells, have thawed antisense therapeutic potential.

We believe our DNAbilize® technology, which is the combination of the protected P-ethoxy antisense DNA backbone with the neutral liposome nanoparticle, is the ideal approach for antisense DNA therapeutics because it overcomes the challenges associated with both antisense stability and intracellular delivery. The P-ethoxy modification used in our DNAbilize® technology is completely sulfur free. We avoid using sulfur-containing antisense because it has been associated with causing liver toxicity and life-threatening bleeding and clotting complications. We prefer neutral lipids to cationic lipids for intracellular delivery because encapsulating the antisense DNA inside a neutral charged lipid bilayer facilitates the delivery and transfer of DNA into the cell to be fluid and gentle. While many companies have focused research on either the DNA stabilization problem or the lipid delivery problem, we are not aware of any company that has developed improvements in both areas. DNAbilize® is truly a stand-alone platform because, as demonstrated by our published preclinical studies, it allows for high doses of drug products to be delivered throughout the entire body while minimizing toxicity. This allows our research and development efforts to focus on drug targets rather than on indications because the DNAbilize® system should not be limited in what types of indications it can treat. As such, we believe that DNAbilize® represents the first ever antisense therapeutic approach that can successfully treat hematological and systemic diseases.

Because of our unique ability to address unmet needs in hematological malignancies, our lead drug candidates focus on cancers of the blood and lymph. Our lead drug candidate, prexigebersen, targets the protein Grb2, a bridging protein between activated and mutated cellular kinases and the proteins involved in cell propagation, and in particular, the Ras protein. When mutations occur that activate these kinases, the cell propagates uncontrollably, via Grb2, and this results in disease progression. Inhibition of Grb2 interrupts this pathway and shuts off propagation signals.

The efficacy of prexigebersen in combination with standard of care therapies is being evaluated in an amended Phase 2 clinical trial for AML patients. The multi-site trial is anticipated to be conducted at ten clinical sites in the U.S.

Our second drug candidate, BP1002, targets the protein Bcl-2. Bcl-2 is an anti-apoptotic member of the Bcl-2 family of proteins that regulate cell death. Overexpression of Bcl-2 results in deregulated cell survival in cancer cells, thus reducing their sensitivity to many of the drugs currently used in the clinic, which mediate their therapeutic effects (at least in part) through the activation of the Bcl-2-regulated apoptotic pathway. The Phase 1 clinical trial will evaluate the safety of BP1002 in refractory/relapsed lymphoma and CLL patients. The Phase 1 clinical trial is being conducted at several leading cancer centers, including MD Anderson Cancer Center and the Georgia Cancer Center. Additionally, a Phase 1/1b clinical trial will evaluate the ability of BP1002 to treat

refractory/relapsed AML patients. The Phase 1/1b clinical trial is anticipated to be conducted at several leading cancer centers in the United States, including the Weill Medical College, MD Anderson Cancer Center and the Georgia Cancer Center.

The intended indications of our two other drug candidates, prexigebersen-A and BP1003, are in solid tumors. Safety and efficacy of prexigebersen-A in combination with paclitaxel will be investigated in patients with recurrent ovarian or endometrial cancer. Safety and efficacy of BP1003 in combination with gemcitabine will be investigated in patients with refractory, metastatic pancreatic cancer.

Strategy

Our strategy is to develop our lead candidates, prexigebersen, prexigebersen-A, BP1002 and BP1003, for multiple indications where the pathways involving Grb2, Bcl-2 and STAT3, respectively, are utilized to promote cancer growth, survival, angiogenesis and tumor surveillance evasion. Using DNAbilize® technology, we plan to develop therapeutics to a wide range of diseases and disorders independently and in partnership with others. The key elements of our strategy include:

(1) **Develop prexigebersen for treatment of AML and MDS in combination therapies.** The efficacy of prexigebersen, our first drug candidate, is being assessed in a Phase 2 study in three cohorts of AML patients. The first cohort enrolls untreated AML patients, and the second cohort enrolls relapsed/refractory AML patients. Both the first and the second patient cohorts will be treated with the triple combination of prexigebersen, decitabine and venetoclax. The third patient cohort, which enrolls relapsed/refractory AML patients who are venetoclax-resistant or -intolerant, will be treated with the two-drug combination of prexigebersen and decitabine. The Company expects to design a clinical trial in the future evaluating MDS patients with prexigebersen.

(2) **Develop prexigebersen-A for treatment of solid tumors.** Preclinical studies demonstrating that prexigebersen-A enhances the efficacy of paclitaxel (a standard of care) in ovarian and endometrial cancer models have been published in the scientific journal Oncotarget in July 2020. In late 2019, we filed an IND application to initiate a Phase 1 clinical trial of prexigebersen-A in patients with recurrent solid tumors. On October 27, 2021, we announced that the FDA cleared the IND application for prexigebersen-A for the initial Phase 1/1b clinical trial, which allows us to proceed with next steps to open the clinical trial. This trial is expected to be conducted at several leading cancer centers and will evaluate the safety of prexigebersen-A in these patients. Assuming positive Phase 1 results, we expect that we would advance to a Phase 1b clinical trial of prexigebersen-A in combination with paclitaxel in patients with recurrent ovarian or endometrial cancer.

(3) **Develop BP1002 for lymphoma and CLL**. The safety, pharmacokinetics and efficacy of BP1002, our second drug candidate, is being evaluated in a Phase 1 clinical trial in refractory/relapsed lymphoma and CLL patients. The Phase 1 clinical trial is being conducted at several leading cancer centers, including MD Anderson Cancer Center and the Georgia Cancer Center and is now open for enrollment. On November 19, 2020, we announced the enrollment and dosing of the first study patient.

(4) **Develop BP1002 for refractory/relapsed AML patients, including those who have relapsed from venetoclax.** The Bcl-2 inhibitor venetoclax is used in frontline combination therapies to treat elderly AML patients; however, venetoclax resistance has been observed. A recent study found that AML patients who had relapsed from frontline venetoclax-based treatment had a very poor prognosis, with a median survival of less than 3 months. Since venetoclax and BP1002 utilize different mechanisms of action, we believe that BP1002 may be a potential treatment for venetoclax-relapsed AML patients. Preclinical studies suggest that the combination of BP1002 with decitabine is efficacious in venetoclax-resistant cells. On August 24, 2021, we announced that the FDA cleared an IND application for BP1002 for an initial Phase 1/ 1b clinical trial that will evaluate the ability of BP1002 to treat refractory/relapsed AML patients, including those who have relapsed from venetoclax. The Phase 1/1b clinical trial is anticipated to be conducted at several leading cancer centers in the United States, including the Weill Medical College, MD Anderson Cancer Center and the Georgia Cancer Center.

(5) **Develop BP1003 for pancreatic cancer, NSCLC and AML**. Our third drug candidate, BP1003, targets the STAT3 protein and is currently in IND enabling studies as a potential treatment of pancreatic cancer, NSCLC and AML. We successfully completed several IND enabling studies of BP1003 in 2021 and expect to complete one additional IND enabling study in 2022. If that additional study is successfully completed, our goal is to file an IND in 2022. Based on

the filing of the IND, we expect to initiate the first-in-humans Phase 1 study of BP1003 in patients with refractory, metastatic solid tumors, including pancreatic cancer and NSCLC.

(6) **Expand DNAbilize® to evaluate targets beyond cancer.** We plan to apply the DNAbilize® delivery technology template to new protein targets that meet scientific, preclinical and commercial criteria and file new patents on these targets. We expect that these efforts will include collaboration with scientific key opinion leaders in the field of study and include developing drug candidates for diseases other than cancer. Our patent portfolio currently includes three issued patents in the U.S. that protect the platform technology for DNAbilize®.

(7) **Establish DNAbilize® as the antisense drug delivery method of choice by forming partnerships with pharmaceutical and academic clinical research labs.** We plan to utilize our business and scientific expertise to identify potential partners and initiate a wide-ranging, proactive licensing program that will include co-development of specific liposomal antisense drug candidates, licensing the delivery template for outside development of one or more liposomal antisense drug candidates or an out-license of a partially developed drug for final development and marketing.

Overview of Drug Candidates

The historical perspective of cancer treatments has been the use of drugs that affect the entire body. Advances in the past decades have shifted to treating the tumor tissue itself. One of the main strategies in these developments has been targeted therapy, involving drugs that are targeted to block the expression of specific disease-causing proteins while having little or no effect on other healthy tissues. We believe that nucleic acid drug products, specifically antisense, are a promising field of targeted therapy. Development of antisense as cancer drugs, however, has been limited by the lack of a suitable method to deliver antisense drugs to cancer cells with high uptake into the cancer cells without causing toxicity to non-cancer cells. Our currently licensed DNAbilize® neutral-lipid based liposome technology is designed to overcome these limitations. We have published preclinical studies demonstrating that our DNAbilize® technology could efficiently deliver antisense therapeutics to mouse models of hematological malignancies and solid tumors, decrease target proteins production and suppress tumor progression. In addition, to date, no adverse effects attributed to the study drugs have been observed in our leukemia and lymphoma clinical trials.

PREXIGEBERSEN

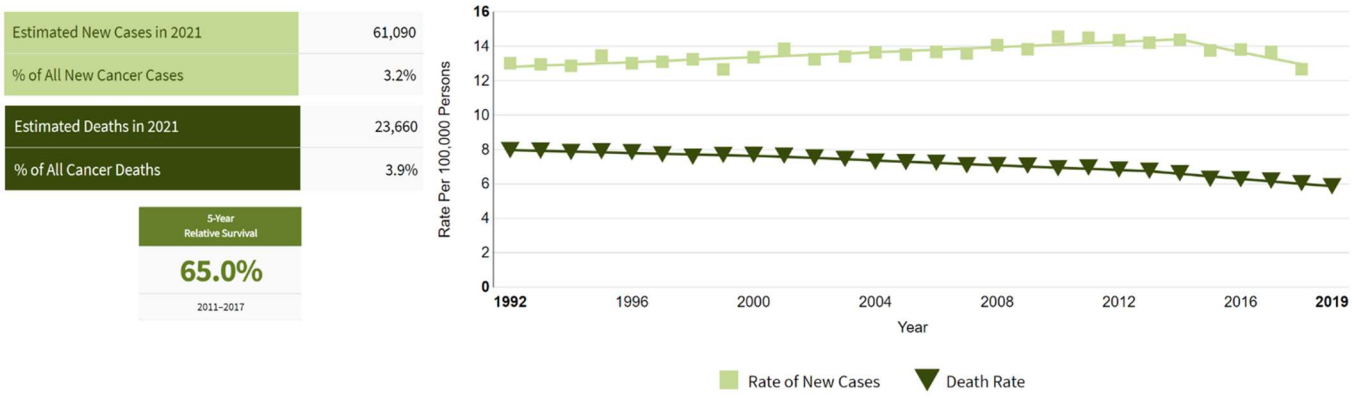
Prexigebersen is targeted at the protein Grb2. Antisense inhibition of Grb2 interrupts the signals between mutated and activated receptors that connect to a well-known cancer associated switch called Ras protein. Inhibition of Grb2 suppresses cancer cells propagation and does not result in adverse events typically observed with receptor inhibitors or Ras pathway inhibitors. We believe that prexigebersen has the potential to be an ideal combination for any number of cancer therapeutics where the Ras pathway is aberrantly activated and patient fitness is a major concern, such as in AML.

Indications for Acute Myeloid Leukemia (AML), Myelodysplastic Syndrome (MDS)

AML - Background and Common Treatments. AML is the rapid accumulation of immature myeloid cells in the blood, resulting in a drop of the other cell types such as red blood cells and platelets. The expansion of immature monocytes leaves the patient unable to fight infection. If AML is left untreated, it usually results in death within three months. AML incidence increases with age, with more than 50% of the cases in people age 60 or older. AML is the most common acute leukemia in adults, and the National Cancer Institute estimates that approximately 20,000 new cases occur each year (Figure 3). The cure rate is between 5 to 15% in older adults, and those who cannot receive the standard course of chemotherapy have an average survival rate of five to ten months. Prior to venetoclax approval, the frontline low-intensity therapies for elderly AML patients were LDAC, decitabine or azacytidine. Venetoclax (a Bcl-2 inhibitor) is approved for newly diagnosed AML patients aged 75 years and older or adults who cannot be treated with intensive induction chemotherapy. Venetoclax is used in combination with LDAC, decitabine or azacytidine. Mutation in the Bcl-2 binding domain, which reduces venetoclax's ability to bind to Bcl-2, has been linked with venetoclax resistance

in CLL patients. Such venetoclax resistance may also occur in AML patients. AML remains an area of high unmet need for both the relapsed and the de novo elderly population who are typically ineligible for induction therapy.

Figure 3. Basic Statistics for AML



MDS - Background and Common Treatments. MDS is a bone marrow disease, characterized by a reduced number of mature blood cells. MDS is diagnosed in about 15,000 people in the United States ("U.S.") yearly. MDS patients are stratified into different risk groups. Higher risk MDS patients have a survival of less than two years and, if untreated, can evolve into secondary AML. Secondary AML patients are often older and treated with decitabine or azacytidine. Higher risk MDS and secondary AML patients who have progressed from decitabine or azacytidine have very poor prognosis. Novel treatment strategies for these patients are needed. The Company expects to design a clinical trial in the future evaluating MDS patients with prexigebersen in combination with decitabine.

Prexigebersen Development and Treatment for Leukemia. The safety, pharmacokinetics and efficacy of our lead DNAbilize® antisense drug candidate, prexigebersen, was assessed in patients having AML, CML, MDS or ALL in a Phase 1 trial. The Phase 1 clinical trial was a dose-escalating study to determine the safety and tolerability of escalating doses of prexigebersen. Additionally, the pharmacokinetics and anti-leukemic effects, including down-regulation of the target Grb2 protein in patient samples, of the drug candidate were determined. Results of the clinical study were published in the scientific journal Lancet Haematology in 2018.

Phase 1 Clinical Trial

Two new assays to provide scientific proof of concept of the delivery technology were developed in the Phase 1 clinical trial. The first assay involved a method to measure down-regulation of the target protein in a patient blood sample that was achieved. The measurement provided critical proof that DNAbilize® neutral liposome delivery technology delivered the drug substance to the cell and was able to transport it across the cell membrane into the interior to block cellular production of the Grb2 protein. The second assay involved a novel detection method for the drug substance in blood samples to assess the pharmacokinetics of the drug.

In August 2013, we announced that our DNAbilize® liposomal delivery technology achieved a major milestone in the development of antisense therapeutics based on a scientific assay confirming that treating patients with our drug candidate prexigebersen inhibits the Grb2 disease-causing target protein in patients with blood cancers (Figure 4). Inhibition of the disease-causing protein has the effect of down regulating the disease. This will allow for prexigebersen to be used potentially in combination with current frontline treatments. This discovery also points to the potential use of a liposomal antisense treatment as a standalone treatment to transform and manage a disease that has a disease-causing protein as a chronic disorder. This accomplishment is a potentially significant breakthrough for antisense therapeutics, whose development, to date, as a class of therapeutics has been severely limited by a lack of a systemic delivery mechanism that can safely distribute the drug throughout the body and deliver the antisense drug substance across the cell membrane into the interior of the cell. Further, we expect that scientific proof of principle for DNAbilize® may lead to licensing and business development opportunities, supporting our business model.

Inhibition of Target Grb2 Protein

- Grb2 levels were compared to baseline prior to treatment.
- By end of treatment, prexigebersen decreased Grb2 in 10 out of 12 samples (83%) tested (average reduction 50%).
- Phosphorylated ERK (pERK, extracellular signal related kinase), a protein downstream of the Ras protein, was decreased in 58% of samples.

Figure 4. Grb2 Protein and Downstream pERK are Downregulated in Prexigebersen Treated Patient's Cells
Grb2 levels decreased in 10 out of 12 patient samples by end of treatment (EOT)
pErk levels decreased in 7 of 12 patient samples by EOT

Subject	Prexigebersen (mg/m^2)	Cohort	Grb2 Decrease (EOT)	pERK Decrease (EOT)
22	20	3	57 %	— %
23	20	3	28 %	45 %
24	20	3	47 %	35 %
25	40	4	54 %	91 %
26	40	4	— %	— %
27	40	4	34 %	27 %
28	60	5	30 %	54 %
29	60	5	65 %	— %
30	60	5	43 %	47 %
31	90	6	— %	— %
32	90	6	91 %	63 %
34	90	6	40 %	— %

A Phase 1 clinical trial is typically ended when a maximum tolerated dose ("MTD") is encountered. However, due to the lack of toxicity of prexigebersen, a MTD was not observed. Lack of toxicity is a major advantage for the drug candidate prexigebersen since it allows higher levels of drug to be administered to the patient, increasing the potential therapeutic benefit. During the Phase 1 trial, 80% of the evaluable patients had refractory/relapsed AML, having failed at least 6 prior therapies. In our study, 83% of patients showed decreased circulating blasts and anti-leukemic activity and eight patients stabilized for extended treatments.

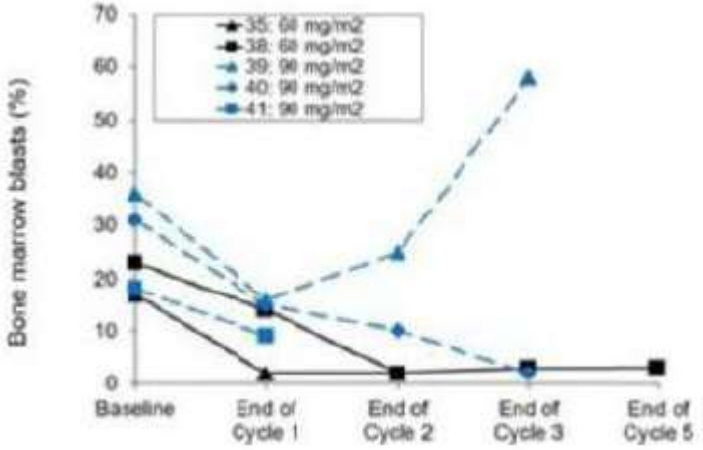
Phase 2 Clinical Trials

On February 9, 2015, we announced that we began enrollment into the combination therapy Phase 1b clinical trial for prexigebersen in patients with AML. The combination therapy Phase 1b clinical trial consisted of two dosing cohorts of prexigebersen (60 mg/m^2 and 90 mg/m^2) to test the safety profile of treating AML patients with prexigebersen in combination with LDAC. Patients ineligible for intensive induction therapy are currently treated with LDAC.

An important outcome of the Phase 1b clinical trial was the ability to assess the pharmacokinetics of the drug. On June 6, 2016, we announced that no dose limiting toxicities were observed in patients treated with the combination therapy of prexigebersen and LDAC. Of the six evaluable patients from the Phase 1b clinical trial, four patients completed more than two cycles of treatment, three patients achieved CR and two patients had over 50% decrease in bone marrow blast counts (Figure 5). Pharmacokinetics of prexigebersen demonstrated a half-life at 60 mg/m^2 of 30 hours, significantly better than the 90 mg/m^2 dose. The final analysis of

these data, along with the demonstrated reductions in bone marrow blasts, suggested that 60 mg/m^2 is the appropriate dose for use in the Phase 2 trial.

Figure 5. Five out of six patients in cohorts 7 and 8 receiving the combination prexigebersen + LDAC have greater than 50% decrease in bone marrow blasts



A summary of the clinical trial results for the Phase 1 monotherapy for indications of AML, CML, MDS and ALL, and Phase 1b combination therapy for prexigebersen for indications of AML is shown in Figure 6 below. The first six cohorts, patients 001 to 034, were treated in the Phase 1 clinical trial using prexigebersen as a monotherapy. The seventh cohort, patients 035, 037 and 038, were treated in our Phase 1b clinical trial evaluating the combination therapy of 60 mg/m^2 prexigebersen. The eighth cohort, patients 039, 040 and 041, were treated with combination therapy of 90 mg/m^2.

Figure 6. Summary Cohorts 1-8 Prexigebersen Clinical Trial Phase 1 and 1B

Patients	Diagnosis	Peripheral or bone marrow blast %			Reason Discontinued	Cycles Completed
		Baseline	Nadir	Off-Tx		
1	CML	51	No	97	DLT	<1
6	AML	15	2	5	PD	5
7	MDS	8	4	6	PD	5
10	AML	23	10	10	PD	1
11	CML	7	No	50	PD	1
14	AML	48	5	21	PD	1
15	AML	54	31	72	PD	1
20	AML	76	5	63	PD	1
21	AML	71	43	74	PD	2
22	AML	1	—	1	PD	2
23	MDS	NE	NE	NE	PD	1
24	MDS	—	—	—	PD	5
25	AML	10	3	19	PD	2
26	AML	11	No	80	PD	1
27	AML	93	No	97	PD	1
28	AML	96	93	98	PD	1
29	AML	35	7	24	PD	1
30	AML	51	17	82	PD	1
31	AML	17	No	17	PD	1
32	AML	24	22	22	PD	2
34	AML	66	ND	ND	PD	1
35	AML	17	2	2	CRi	1
37	AML	25	33	ND	PD	1
38	AML	23	2	3	CR	5
39	AML	36	16	58	SD	3
40	AML	31	2	2	CR	3
41	AML	18	9	14	SD	3

Nadir: the lowest point, Off-TX: off treatment, No: no reduction in blasts, DLT: dose limiting toxicity, PD: progressive disease, NE: not enough sample to evaluate, ND: not done, CR_i: complete remission with incomplete hematologic recovery, CR: complete remission, SD: stable disease

Results from the Phase 1b clinical trial demonstrated it is safe to add prexigebersen to LDAC, which appears to yield better response rates in this AML patient population. On November 2, 2016, we announced that the first patient in the efficacy portion of the Phase 2 trial was dosed. The full trial design includes approximately 54 evaluable patients with an interim analysis to be performed after 19 patients are treated with the combination. The multi-site trial was conducted at leading cancer centers, among them are Weill Medical College, Baylor Scott & White Health, The University of Kansas, New Jersey Hematology Oncology Associates, West Virginia University/Mary Babb Randolph Cancer Center, and MD Anderson Cancer Center.

Thirty-three patients were pre-screened for the efficacy portion of the Phase 2 prexigebersen + LDAC combination study. Thirty patients were enrolled and 17 patients were deemed evaluable. The interim data that we released on March 6, 2019 showed that 11 (65%) of the 17 evaluable patients had a response, including five (29%) who achieved CR, including one CR_i and one morphologic leukemia free state, and six (35%) stable disease responses, including two patients who had greater than a 50% reduction in bone marrow blasts. The efficacy data from the 17 evaluable patients was very favorable compared to the reported CR, CRp and CRi rates of 7 to 13% with LDAC treatment alone. Importantly, through investigation by the principal investigators, it was observed that 68% of patients were secondary AML patients, a difficult class to treat.

Results to date have shown prexigebersen, with its efficacy and excellent safety profile, to be an effective combination candidate with frontline therapy. However, DNA hypomethylating agents are now the most frequently used agents in the treatment of elderly AML patients in the U.S. and Europe. As a result, we amended Stage 2 of the Phase 2 trial in AML to remove the combination treatment of prexigebersen and LDAC and replace it with the combination treatment of prexigebersen and decitabine. Since decitabine is also used as a treatment for relapsed/refractory AML patients, a cohort of relapsed/refractory AML patients was also added to the study.

We believe the approval of the frontline venetoclax and decitabine combination therapy provides an opportunity for combining prexigebersen with the combination therapy for the treatment of *de novo* AML patients. Preclinical testing of prexigebersen with venetoclax and decitabine demonstrated the potential to enhance efficacy of the frontline treatment combination. The triple combination of prexigebersen, venetoclax and decitabine showed significant improvement in decreasing the viability of three of the four AML cell lines tested. Bio-Path's approved amended Stage 2 for this Phase 2 clinical trial has three cohorts of patients. The first two cohorts will treat patients with the triple combination of prexigebersen, decitabine and venetoclax with the first cohort including untreated AML patients and the second cohort including relapsed/refractory AML patients. Finally, the third cohort will treat relapsed/refractory AML patients who are venetoclax-resistant or -intolerant with the two-drug combination of prexigebersen and decitabine.

The first step in establishing the amended Stage 2 of the Phase 2 trial in AML was demonstrating the safety of treating patients with the two-drug combination of prexigebersen and decitabine, which was reported in November 2019. On August 13, 2020, we announced the enrollment and dosing of the first patient in the amended Stage 2 of the Phase 2 clinical study. The safety segment of Stage 2 of the Phase 2 clinical trial comprised six evaluable patients who were treated with the combination of prexigebersen and decitabine. Although the treatment combination of prexigebersen and decitabine was not the treatment planned for the efficacy evaluation of Stage 2 of the Phase 2 clinical trial, the efficacy profile in this safety segment of the study was encouraging with 50% of patients having a response, including two complete responses (33%) with incomplete hematologic recovery and one patient (17%) showing partial response. For reference, in this class of AML patients, the complete response rate to treatment with decitabine alone is approximately 20%.

On April 5, 2021, we announced the successful completion of the safety run-in of Stage 2 of the Phase 2 clinical study. In the safety run-in of the triple combination, six evaluable patients were treated with the combination of prexigebersen, decitabine and venetoclax. These patients included four relapsed/refractory AML patients, and two newly diagnosed AML patients. In the preliminary safety data review, five of the patients (83%) responded to treatment, including four (67%) achieving CR and one (17%) achieving CRi. Recent publications provide that CR rates to combination treatment with decitabine and venetoclax (but without prexigebersen) are 42 to 52% for relapsed/refractory AML patients and 0 to 39% for relapsed/refractory secondary AML patients. Response rates to frontline treatment with decitabine and venetoclax (but without prexigebersen) are 62 to 71% for newly diagnosed AML patients. These preliminary data, presented at the 2021 American Society of Hematology Annual Meeting, showed the treatment was well-tolerated and there were no dose limiting toxicities attributed to prexigebersen. Three patients remained on treatment for more than one cycle.

Development of new therapeutics for AML can meet currently unmet needs for patients who have very few treatment options due to age, fitness or treatment-resistance of advanced genetically unstable cells. Elderly patients unfit to receive a stem cell transplant or induction therapy face a likelihood of relapse to a more resistant leukemia. Prexigebersen and DNAbilize® technology offer new hope for achieving remission for fragile populations. We believe that the combination of prexigebersen with frontline chemotherapy can provide a way to treat cancer without added toxicity so that the patient can remain under treatment long enough to reach complete remission.

PREXIGEBERSEN-A

Data supports a prominent role of Grb2 in the progression of solid tumors, and overexpression of Grb2 has been associated with chemosensitivity, poor prognosis and advanced disease in several malignancies including gynecologic malignancies.

Indications for Solid Tumors (e.g., Ovary, Endometrium)

Ovarian cancer is one of the most common type of gynecologic malignancies, with 50% of all cases occurring in women older than 63 years. It is the fifth most frequent cause of cancer death in women. In the U.S., 21,410 new cases of and 13,770 deaths from ovarian cancer were expected in 2021. Around 70% of patients diagnosed with ovarian cancer will have a recurrence. Recurrent ovarian cancer is treatable but rarely curable. The average duration of survival after recurrence of ovarian cancer is less than 2 years. The 5-year survival rate for patients with recurrent ovarian cancer following standard salvage chemotherapy treatment is less than 10%. Given the poor outcomes of treatment for ovarian cancer, novel drug treatments are urgently needed.

Endometrial cancer is the most common gynecologic malignancy in the U.S. In the U.S., 66,570 new cases of and 12,940 deaths from endometrial cancer were expected in 2021. The majority of cases are diagnosed at an early stage and are amenable to

treatment with surgery alone. However, approximately 50% of advanced stage endometrial cancers will recur. Recurrent endometrial cancer is incurable with currently available standard therapies. The median survival for patients with recurrent endometrial carcinoma hardly exceeds 12 months. Novel drug treatments for recurrent endometrial carcinoma are urgently needed.

Development and Treatment for ovarian and endometrial cancer

Grb2 may be a novel potential therapeutic target for ovarian and endometrial cancer, and prexigebersen-A may provide clinical benefit against these gynecologic malignancies. Preclinical experiments were conducted in collaboration with leaders in the field of ovarian cancer at MD Anderson Cancer Center. Results of the preclinical study were published in the scientific journal Oncotarget in July 2020. Prexigebersen-A effectively penetrated ovarian tumors and decreased target Grb2 protein level in preclinical ovarian and endometrial tumor models. Prexigebersen-A was demonstrated to reduce tumor burden both as a monotherapy and in combination with paclitaxel, a therapy commonly used to treat patients with advanced ovarian or endometrial cancer. In late 2019, we filed an IND application to initiate a Phase 1 clinical trial of prexigebersen-A in patients with advanced or recurrent solid tumors. On October 27, 2021, we announced that the FDA cleared the IND application for prexigebersen-A for the initial Phase 1/1b clinical trial, which allows us to proceed with next steps to open the clinical trial. This trial is expected to be conducted at several leading cancer centers and will evaluate the safety of prexigebersen-A in these patients. Assuming positive Phase 1 results, we expect that we would advance to a Phase 1b clinical trial of prexigebersen-A in combination with paclitaxel in patients with recurrent ovarian or endometrial tumors.

Indications for Triple Negative Breast Cancer (TNBC) and Inflammatory Breast Cancer (IBC)

TNBC and IBC - Background and Common Treatments. Approximately 15 to 20% of breast cancers fall into the category of triple-negative. TNBC tumors do not express estrogen receptors, progesterone receptors, and low human epidermal growth factor receptor 2 (HER2). These negative indicators mean that the growth of the cancer is not supported by the hormones estrogen and progesterone, or by the presence of HER2 receptors. Therefore, TNBC does not respond to hormonal therapy or therapies that target HER2 receptors. In addition, TNBC tumors are very aggressive. IBC is a rare and very aggressive type of breast cancer that accounts for 2 to 5% of all breast cancers. A lack of targeted treatments for these types of breast cancer has led to development of new therapeutics currently in clinical trials. Overexpression of receptor tyrosine kinases has been reported for TNBC and IBC. Since Grb2 is vital in the cancer signaling of receptor tyrosine kinases, the Company and collaborators at MD Anderson Cancer Center are interested in developing prexigebersen-A as a potential treatment for TNBC and IBC.

BP1002

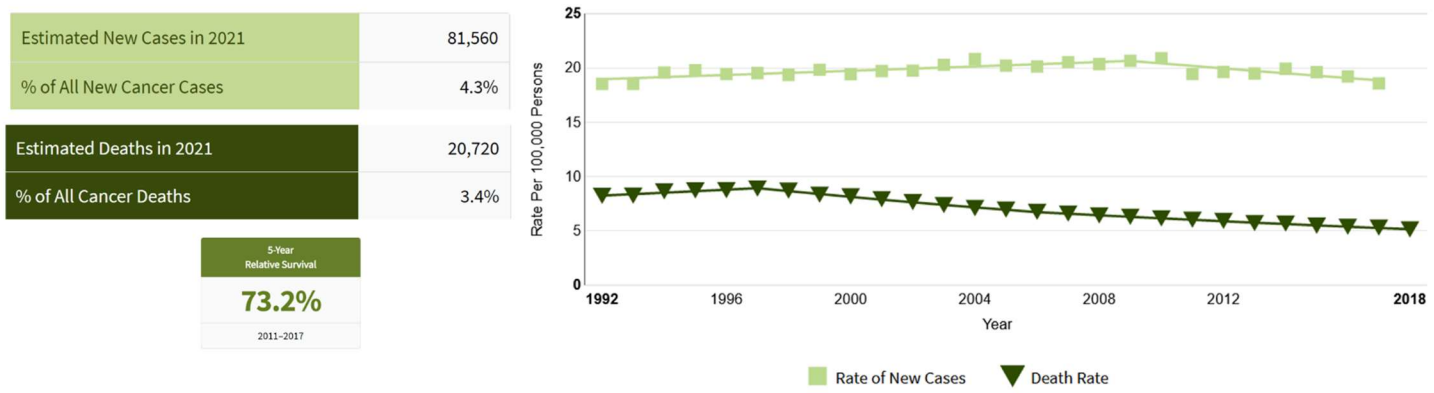
BP1002, also known by its scientific name as Liposomal Bcl-2, is our second liposome delivered antisense drug candidate. BP1002 is intended to target lymphoma, CLL, AML and certain solid tumor markets. We believe that BP1002 has the potential to treat 40 to 60% of solid tumors.

Bcl-2 is a protein that is involved in regulating apoptosis, or programmed cell death. Apoptosis is a physiologic mechanism of cell turnover by which cells actively commit suicide in response to aberrant external signals. Over-expression of Bcl-2 prevents the induction of apoptosis in response to cellular insults such as treatment with chemotherapeutic agents. Bcl-2 is over-expressed in more than 90% of follicular lymphoma (FL) due to a chromosomal rearrangement and is the key factor in the initiation of this malignancy. Bcl-2 was also found to contribute to the pathophysiology of other lymphomas, such as CLL, mantle cell lymphoma, Waldenströms macroglobulinemia and double-hit diffused large B-cell lymphoma (DLBCL), all of which are subtypes of non-Hodgkin's lymphoma (NHL).

Non-Hodgkin's Lymphoma - Background and Common Treatments. Lymphoma can start anywhere in the body where lymph tissue is found. The major sites of lymph tissue are lymph nodes, bone marrow, spleen, thymus, adenoids and tonsils and the digestive tract. NHL is a term used for many different types of lymphoma that share some common characteristics. In the U.S., approximately 81,560 new cases of and 20,720 deaths from NHL were expected in 2021 (Figure 7). Approximately 40% of NHLs are indolent lymphomas and approximately 60% are more aggressive lymphomas. Indolent lymphomas grow and spread slowly. Some indolent lymphomas might not need to be treated right away but can be monitored closely instead. On the other hand, aggressive lymphomas

usually need to be treated right away, as they grow and can spread quickly to other parts of the lymph system or to other parts of the body, such as the liver, brain or bone marrow.

Figure 7. Basic statistics of Non-Hodgkin's Lymphoma



BP1002 - Development and Treatment for lymphoma. On December 22, 2014, we announced that we initiated development of BP1002 as a treatment for refractory/relapsed patients with NHL (including CLL, mantle cell lymphoma, Waldenströms macroglobulinemia, DLBCL, peripheral T-cell lymphoma, cutaneous T-cell lymphoma, and marginal zone lymphoma) and Hodgkin's lymphoma.

Therapies that directly and specifically block or inhibit protein synthesis of Bcl-2 could be transformative for NHL. Previous attempts at a Bcl-2 antisense by Genta Inc. and ProNAi failed to show an improvement in remission or overall survival rates. The Genta antisense was a phosphorothioate DNA with dose-limiting toxicity and it also did not have a lipid delivery mechanism to aid in prevention of clearance by the liver, reducing the levels of antisense reaching diseased cells. The ProNAi antisense was administered with an anionic, pH-tunable liposome. The drug was tolerable but its low response rate in DLBCL patients in a Phase 2 study prompted the company to discontinue further clinical development. We believe that BP1002 overcomes the failures of previous antisense attempts at inhibiting Bcl-2. With BP1002, more drug substance can reach the lymphoma cells so that the cancer cells can be treated with a safe and therapeutically relevant dose. The Bcl-2 inhibitor venetoclax was approved by the FDA in June 2018 for the treatment of patients with CLL and small lymphocytic leukemia (SLL) who have received at least one prior therapy. In May 2019, the FDA approved venetoclax in combination with obinutuzumab for the treatment of adult CLL and SLL patients with previously untreated disease. However, treatment with venetoclax can lead to the development of drug resistance, resulting in disease recurrence. One of the proposed mechanisms of venetoclax resistance is acquired mutations in Bcl-2, which reduce venetoclax's ability to bind and inhibit Bcl-2. Because BP1002 activity is based on blocking the Bcl-2 messenger RNA and BP1002 targets Bcl-2 at a site different from venetoclax, we expect BP1002 to overcome such venetoclax resistance mechanism and be an effective approach for patients who have relapsed from venetoclax. Preclinical studies suggest that the combination of BP1002 with decitabine is efficacious in venetoclax-resistant lymphoma cells. An abstract of the preclinical study was presented at the 2021 American Association for Cancer Research Annual Meeting. We believe BP1002 provides a new tool for cancer treatment for not just lymphomas, but also many cancers for which Bcl-2 expression is driving cell survival. The introduction of a new, non-toxic, and specific Bcl-2 inhibitor could be a major advance in cancer therapeutics.

On November 21, 2019 we announced that the FDA cleared an IND application for BP1002. An initial Phase 1 clinical trial will evaluate the ability of BP1002 to treat refractory/relapsed lymphoma and CLL patients. The Phase 1 clinical trial is being conducted at several leading cancer centers, including MD Anderson Cancer Center and the Georgia Cancer Center and is now open for enrollment. On November 19, 2020, we announced the enrollment and dosing of the first patient in the Phase 1 clinical trial. Initially, a total of six evaluable patients are scheduled to be treated with BP1002 monotherapy in a standard 3+3 design, with a starting dose of 20 mg/m^2. The approved treatment cycle is two doses per week over four weeks, resulting in eight doses administered over twenty-eight days.

BP1002 - Development and Treatment for AML

The Bcl-2 inhibitor venetoclax is used in frontline combination therapies to treat elderly AML patients; however, venetoclax resistance has been observed. Since venetoclax and BP1002 utilize different mechanisms of action, we believe that BP1002 may be a potential treatment for venetoclax-relapsed AML patients. Preclinical studies, presented as an abstract at the 2021 American Association for Cancer Research Annual Meeting, suggest that the combination of BP1002 with decitabine is efficacious in venetoclax-resistant AML cells. On August 24, 2021, we announced that the FDA cleared an IND application for BP1002 for an initial Phase 1/1b clinical trial that will evaluate the ability of BP1002 to treat refractory/relapsed AML patients, including those who have relapsed from venetoclax. The Phase 1/1b clinical trial is anticipated to be conducted at several leading cancer centers in the United States, including the Weill Medical College, MD Anderson Cancer Center and the Georgia Cancer Center. Gail J. Roboz, M.D., will serve as Principal Investigator for the Phase 1/1b trial.

BP1003

BP1003 is our third liposome delivered antisense drug candidate. BP1003 is a DNAbilize® RNAi nanoparticle containing antisense DNA targeting STAT3, whose elevated expression/activity is associated with a poorer survival outcome for patients with solid tumors, including those of gastric cancer, lung cancer, hepatic cancer, osteosarcoma, prostate cancer and pancreatic adenocarcinoma (PDAC). We believe that a therapeutic that shuts down the STAT3 protein can have significant clinical impact for solid tumors that have elevated expression/activity of STAT3.

Our lead indication for BP1003 is pancreatic cancer due to the severity of this disease and the lack of effective, life-extending treatments. PDAC is a cancer of the exocrine cells of the pancreas. In the U.S. in 2021, approximately 60,430 people were diagnosed with PDAC, and approximately 48,220 died from the disease. It is estimated that less than 11% of PDAC patients survive beyond 5 years, and it is projected that by 2030, PDAC will become the second most lethal cancer behind lung cancer. Treatment of the disease is hampered by the location of the pancreas, which is difficult to reach with conventional therapies and the fibrotic nature of the tumors, which protects them from penetration by chemotherapeutics. We believe a novel and unconventional therapeutic is needed to overcome these barriers to treatment.

While competition for therapeutics that target the STAT3 pathway exist, the competition for specific STAT3 inhibitors is very small. Many peptides designed to bind to STAT3 suffered from poor intrinsic pharmacokinetic properties, including poor cellular permeability and lack of stability in vivo, which curtailed their further development. Even second-generation peptidomimetics have failed to overcome these limitations. Most compounds under development target the pathway upstream of STAT3, such as the JAK2 kinase. However, lack of efficacy of the JAK2 kinase inhibitors was observed in PDAC clinical studies. Ionis Pharmaceuticals, Inc. has developed an antisense DNA-based STAT3 inhibitor called IONIS-STAT3-2.5Rx. It is being evaluated in clinical trials by AstraZeneca under the name AZD9150 for solid tumors and NHL. However, due to the toxicity of the DNA chemistry, thrombocytopenia continues to limit the systemic delivery and efficacy of such compounds for the treatment of cancer. We believe BP1003 avoids these complications.

We hypothesized that the natural lipid delivery vesicle would have unique characteristics that would allow for penetration of the fibrotic stroma to reach the PDAC cells. An abstract of the preclinical study was presented in the 2019 American Association for Cancer Research Annual Meeting. Our preclinical work demonstrated that BP1003 was successful in crossing the scar tissue matrix and delivering antisense drug into the tumor tissue. Subsequent studies evaluating the combination of BP1003 with gemcitabine, a standard of care for PDAC patients with metastatic disease, suggest that the regimen has synergistic anti-tumor effects. We successfully completed several IND enabling studies of BP1003 in 2021 and expect to complete one additional IND enabling study in 2022. If that additional study is successfully completed, our goal is to file an IND in 2022. Based on the filing of the IND, we expect to initiate the first-in-humans Phase 1 study of BP1003 in patients with refractory, metastatic solid tumors, including pancreatic cancer and NSCLC.

We believe that the excellent safety profile of the DNAbilize® chemistry, the novel lipid formula that allows for penetration of the tumor stroma, and the ability to target a single protein with precision, makes BP1003 an ideal candidate for combination with approved treatments to extend survival while maintaining quality of life for the patient.

DNABILIZE®

DNAbilize® technology is available for out-licensing. We intend to apply our drug delivery technology template to new disease-causing protein targets as a means to develop new liposomal antisense drug candidates. A new product identification template was recently approved that defines a process of scientific, preclinical, commercial and intellectual property evaluation of potential new drug candidates for inclusion into our drug product development pipeline. A significant amount of capital is expected to be allocated to in-license promising protein targets that can be developed as new liposomal antisense drug candidates. As we expand, we will look at indications where a systemic delivery is needed and antisense can be used to slow, reverse or cure a disease, either alone or in combination with another drug. Our patent portfolio currently includes three issued patents in the U.S. that protect the platform technology for DNAbilize®, the Company's novel RNAi nanoparticle drugs. We plan to continue our efforts to build protection around our technology as it safeguards our platform technology and target-specific technology, is a deterrent to would-be competitors and creates value around our core competencies.

We are interested in pursuing a wide-ranging, proactive licensing program to include co-development of specific liposomal antisense drug candidates, sub-licensing our delivery template for outside development of liposomal antisense drug candidates or out-licensing a partially-developed drug candidate for final development and marketing.

Research and Development

Our research and development expense primarily consists of third-party clinical, preclinical and manufacturing development activities, salaries and benefits expense and stock-based compensation. As we advance and expand our pipeline of drug candidates, we anticipate our research and development expenses will continue to increase in conjunction with these activities. Research and development expenses incurred during the years ended December 31, 2021 and 2020 were $5.9 million and $6.6 million, respectively.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. Accordingly, we have no ability to internally manufacture the drug candidates that we need to conduct our clinical trials. For the foreseeable future, we expect to continue to rely on third-party manufacturers and other third parties to produce, package and store sufficient quantities of our drug candidates and any future drug candidates for use in our clinical trials. We have entered into agreements with third-party manufacturers for the manufacture of our drug requirements, including agreements for the manufacture of prexigebersen for use in our Phase 2 clinical trial in AML, as well as agreements for the manufacture of prexigebersen-A, BP1002 and BP1003 for use in our Phase 1 clinical trials. However, we may face various risks and uncertainties in connection with our reliance on third-party manufacturers, as discussed in "Item 1A. Risk Factors" of this Annual Report on Form 10-K under the heading "Risks Related to Manufacturing Our Drug Candidates." If the FDA or other regulatory agencies approve any of our drug candidates for commercial sale, we expect that we would continue to rely, at least initially, on third-party manufacturers to produce commercial quantities of such approved drug candidates. However, we may in the future elect to manufacture certain of our drug candidates in our own manufacturing facilities. If we do so, we will require substantial additional funds and need to recruit qualified personnel in order to build or lease and operate any manufacturing facilities.

Sales and Marketing

We currently do not have any commercial drug products or an organization for the sales and marketing of pharmaceutical products. In order to successfully commercialize any drug candidates that may be approved in the future by the FDA or comparable foreign regulatory authorities, we must build our sales and marketing capabilities or make arrangements with third parties to perform these services. For certain drug candidates in selected indications where we believe that an approved product could be commercialized by a specialty sales force that calls on a limited but focused group of physicians, we may commercialize these products ourselves. However, in therapeutic indications that require a large sales force selling to a large and diverse prescribing population, we may enter into arrangements with other companies for commercialization. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable.

Intellectual Property

Patents, trademarks, trade secrets, technology, know-how and other proprietary rights are important to our business. Our success depends in large part on our ability to obtain and maintain patent protection both in the U.S. and in other countries for our drug candidates and on our ability to operate without infringing the proprietary rights of third parties. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents.

We rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. In order to protect our proprietary technology and processes, we also rely in part on confidentiality and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators, sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information nor result in the effective assignment to us of intellectual property, and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information or other breaches of the agreements. In addition, others may independently discover our trade secrets and proprietary information, and in such case we could not assert any trade secret rights against such party. To the extent that we enter into out-license and in-license agreements in the future, our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for their intellectual property, in particular, any patents to which we secure exclusive rights.

We have expanded our intellectual property portfolio by filing patent applications that are applicable to our technology and business strategy. Our patent portfolio currently includes five issued patents in the U.S. and two issued patents in foreign jurisdictions:

Claims Related to DNAbilize®

Patent No.	Title	Date Issued
US 9,744,187	P-ethoxy nucleic acids for liposomal formulation	August 29, 2017
US 10,335,428	P-ethoxy nucleic acids for liposomal formulation	July 2, 2019
US 10,898,506	P-ethoxy nucleic acids for liposomal formulation	January 26, 2021
SG 11201802718P	P-ethoxy nucleic acids for liposomal formulation	May 12, 2021
EA 038277	P-ethoxy nucleic acids for liposomal formulation	August 4, 2021

Compositions and Methods of Use for Specific Drug Targets

Patent No.	Title	Date Issued
US 10,927,379	Combination therapy with liposomal antisense oligonucleotides	February 23, 2021
US 11,041,153	P-ethoxy nucleic acids for STAT3 inhibition	June 22, 2021

We have six additional pending patent applications in the U.S. In addition, we have pending patent applications in key foreign jurisdictions across our six families of applications. We continue our efforts to build protection around our technology as it safeguards our platform technology and target-specific technology, is a deterrent to would-be competitors and creates value around our core competencies.

There can be no assurances that patents related to our existing patent applications or applications we may file in the future will be issued or that any issued patents will provide meaningful protection for our drug candidates, which could materially and adversely affect our competitive business position, business prospects and financial condition.

In the U.S., individual patents extend for varying periods of time depending on the date of filing of the patent application or the date of patent issuance. Generally, patents issued in the U.S. are effective for 20 years from the earliest non-provisional filing date. In addition, a patent term can sometimes be extended to recapture a portion of the term effectively lost during the FDA’s regulatory

review period; however, the restoration period cannot be longer than five years, and the total patent term cannot exceed 14 years following FDA approval.

Employees

We currently employ ten full-time employees. We also have contractual relationships with additional professionals who perform certain medical officer, regulatory, drug development and administrative duties. We believe relations with such professionals and employees are good.

Competition

We are engaged in segments of the pharmaceutical and biotechnology industry that are highly competitive and characterized by rapid and significant technological change. Many large pharmaceutical and biotechnology companies, academic and research institutions, governmental agencies and other public and private research organizations are pursuing the development of novel drugs that target AML, MDS, lymphoma, ovarian and endometrial cancer, pancreatic cancer, and other cancers generally. We face, and expect to continue to face, intense and increasing competition as new products enter the market and advanced technologies become available. Our competitors may discover, develop or commercialize products or other novel technologies that are more effective, safer or less costly than our drug candidates. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for our drug candidates.

Many of our competitors have:

- significantly greater capital, technical and human resources than we have and may be better equipped to discover, develop, manufacture and commercialize drug candidates;
- more experience in drug discovery, development and commercialization, obtaining regulatory approvals and manufacturing and marketing pharmaceutical products;
- drug candidates that have been approved or are in late-stage clinical development; and/or
- collaboration arrangements in our target markets with leading companies and research institutions.

Mergers and acquisitions in the pharmaceutical and biotechnology industry 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, establishing clinical trial sites and patent registration for clinical trials, and acquiring technologies complementary to, or necessary for, our drug candidates and programs.

Competitive products and technological developments may render our drug candidates noncompetitive or obsolete before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and/or the widespread adoption or increased utilization of any vaccine for the diseases we are targeting could render our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for any of our drug candidates, we will face competition based on the safety and effectiveness of our drug candidates, the timing of their entry into the market in relation to competitive products in development, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent position and other factors. If we successfully develop drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful.

Government Regulation

Overview

Government authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, record keeping, packaging, promotion, storage, advertising,

distribution, marketing and export and import of products such as those we are developing. The nature and extent to which such regulations will apply to us will vary depending on the nature of any drug candidates we develop. We anticipate that all of our drug candidates will require regulatory approval by governmental agencies prior to commercialization. This process and subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations will require the expenditure of substantial time and financial resources.

U.S. Drug Development Process

In the U.S., drugs are subject to rigorous regulation by the FDA under the Federal Food, Drug and Cosmetic Act (the "FDCA"), and implementing regulations, as well as other federal and state statutes. Failure by us or our collaborators to comply with the applicable U.S. requirements at any time during the drug candidate development process, approval process or after approval, may subject us to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a new drug may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to FDA's Good Laboratory Practice regulations;
- submission of an IND, which must become effective before human clinical trials may begin and which must include approval by an institutional review board at each clinical site before the trials are initiated;
- performance of adequate and well-controlled human clinical trials according to FDA's Good Clinical Practice ("GCP") regulations to establish the safety and efficacy of the proposed drug for its intended use;
- submission to, and acceptance by, the FDA of a new drug application (an "NDA");
- completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice ("cGMP") regulations to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Pre-Approval Studies

Once a drug candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of drug candidate chemistry, toxicity and formulation, as well as animal studies. Prior to beginning human clinical trials, an IND sponsor must submit an IND to the FDA, which includes submitting the results of the preclinical tests, together with manufacturing information and analytical data. Some preclinical or nonclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the trial. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Even after the 30-day time period, the FDA may impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. The IND application process may be extremely costly and substantially delay the development of our drug candidates for certain indications. Moreover, positive results of preclinical tests will not necessarily indicate positive results in subsequent clinical trials in humans. The FDA may require additional animal testing after an initial IND application is approved and prior to Phase 3 trials.

Clinical trials involve the administration of the IND to volunteers or patients under the supervision of one or more qualified investigators in accordance with FDA's GCP regulations. Clinical trials must be conducted under protocols detailing the objectives of the trial and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. Further, an institutional review board at each institution participating in the clinical trial must review and approve each protocol before any clinical trial commences at that institution. All research subjects must provide informed consent, and informed consent information must be submitted to the institutional review board for approval prior to initiation of the trial. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if adverse events or other certain types of other changes occur.

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

- *Phase 1:* The drug candidate is initially introduced into human subjects or patients with the disease and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some drug candidates for severe or life-threatening diseases, the initial human testing is often conducted in patients.

- *Phase 2:* Involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug candidate for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3:* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, typically at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the drug candidate and provide, if appropriate, an adequate basis for product labeling.

Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or an institutional review board or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk.

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

Our business model relies on developing drug candidates through Phase 2a and either entering into out-license agreements with pharmaceutical licensee partners who will be responsible for post-Phase 2 clinical testing and working with the FDA on necessary regulatory submissions resulting in approval of new drug applications for commercialization, or internally developing a drug candidate through commercialization.

Approval Process

After successful completion of the required clinical trials, an NDA is generally submitted, which is required before marketing of the product may begin in the U.S. The NDA must include the results of drug development, preclinical studies and clinical studies, together with other detailed information, including information on the chemistry, manufacture and composition of the drug. The FDA has 60 days from its receipt of the NDA to review the application to ensure that it is sufficiently complete for substantive review before accepting it for filing and may request additional information rather than accept an NDA for filing. If additional information is requested, the NDA must be resubmitted. 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 submission of an NDA is also subject to the payment of user fees, which may be waived under certain limited circumstances.

The FDA reviews an NDA that has been accepted for filing to determine, among other things, whether a product is safe and effective for its intended use. The approval process for an NDA is lengthy and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA may also refer applications for drug candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee. Before approving an NDA, the FDA will also inspect the facility or facilities where the product is manufactured to determine whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality, purity and stability.

There are various programs that are intended to expedite the development and review of drug candidates, and/or provide for approval on the basis of surrogate endpoints, including Fast Track, breakthrough therapy, priority review and accelerated approval. Even if a drug candidate qualifies for one or more of these programs, the FDA may later decide that the drug candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drug candidates that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs or those that offer meaningful benefits over existing treatments.

Fast Track is a process designed to facilitate the development, and expedite the review of drug candidates to treat serious diseases and fill an unmet medical need. Breakthrough therapy requires preliminary clinical evidence that demonstrates the drug candidate may have substantial improvement on at least one clinically significant endpoint over available therapy. A breakthrough therapy designation conveys all of the Fast Track program features, as well as more intensive FDA guidance on an efficient drug development program. Priority review is designed to give drug candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of 10 months. Although Fast Track, breakthrough therapy and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug candidate and expedite review of the application for a drug candidate designated for priority review. Accelerated approval provides an earlier approval of drugs to treat serious diseases and that fill an unmet medical need based on a surrogate endpoint, which is a laboratory measurement or physical sign used as an

indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a product receiving accelerated approval perform post-marketing clinical trials.

If the FDA evaluations of the application and the manufacturing facilities are favorable, the FDA may issue an approval letter or an "approvable" letter. An approvable letter will usually contain a number of conditions that must be met in order to secure final approval of the NDA and authorization of commercial marketing of the drug for certain indications. An approval letter authorizes commercial marketing of the drug with specific prescribing information for a specific indication. As a condition of NDA approval, the FDA may require post-approval testing, including Phase 4 trials, and surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling or distribution restrictions which can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems occur after the product reaches the market. The FDA may also refuse to approve the NDA or issue a "not approvable" letter outlining the deficiencies in the submission and often requiring additional testing or information.

To date, we have not submitted a marketing application for any drug candidate to the FDA or any foreign regulatory agency, and none of our drug candidates have been approved for commercialization in any country. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to complete clinical trials and for the FDA's review processes is uncertain and typically takes many years. Our analysis of data obtained 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 unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials, and FDA regulatory review.

Timing to Approval

We estimate that it generally takes 10 to 15 years or possibly longer to discover, develop and bring to market a new pharmaceutical product in the U.S. as outlined below:

Phase:	Objective:	Estimated Duration:
Discovery	Lead identification and target validation.	2 to 4 years
Preclinical	Initial toxicology for preliminary identification of risks for humans; gather early pharmacokinetic data.	1 to 2 years
Phase 1	Test for safety, dosage tolerance, absorption, metabolism, distribution and excretion.	1 to 2 years
Phase 2	Identify possible adverse effects and safety risks; preliminarily evaluate the efficacy of the drug candidate for specific targeted diseases; determine dosage tolerance and optimal dosage.	2 to 4 years
Phase 3	Further evaluate dosage, clinical efficacy and safety in an expanded patient population, typically at geographically dispersed clinical study sites	2 to 4 years
FDA approval	Approval by the FDA to sell and market the drug for the approved indication.	6 months to 2 years

A drug candidate may fail at any point during this process. Animal and other non-clinical studies typically are conducted during each phase of human clinical trials.

Our business model is primarily focused on the preclinical to Phase 2a interval. This greatly reduces the time frame for us from in-license of a new, preclinical stage drug candidate to be developed to out-licensing to a pharmaceutical partner.

Post-Approval Studies

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. 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 FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the drug;
- providing the FDA with updated safety and efficacy information;
- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- complying with certain electronic records and signature requirements; and
- complying with FDA promotion and advertising requirements.

Drug manufacturers and their subcontractors are required to register their establishments with the FDA and some state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our drug candidates. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our drug candidates. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Foreign Regulations

Whether or not we obtain FDA approval for a drug candidate, we must obtain the requisite approvals from regulatory authorities in non-U.S. countries prior to the commencement of clinical trials or marketing of our products in those countries. Certain countries outside of the U.S. have a process that requires the submission of a clinical trial application (“CTA”), much like an IND, prior to the commencement of human clinical trials. In the E.U., for example, a CTA must be submitted to the competent national

health authority and to independent ethics committees in each country in which a company intends to conduct clinical trials. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed in that country.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country, but typically takes several years and requires significant resources. In all cases, the clinical trials must be conducted in accordance with GCP and other applicable regulatory requirements.

To obtain regulatory approval of an investigational drug under E.U. regulatory systems, we must submit a marketing authorization application. This application is similar to the NDA in the U.S., with the exception of, among other things, country-specific document requirements. Drugs can be authorized in the E.U. by using (i) the centralized authorization procedure, (ii) the mutual recognition procedure, (iii) the decentralized procedure or (iv) national authorization procedures.

The EMA implemented the centralized procedure for the approval of human drugs to facilitate marketing authorizations that are valid throughout the E.U. This procedure results in a single marketing authorization granted by the European Commission that is valid across the E.U., as well as in Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for certain human drugs including those that are: (i) derived from biotechnology processes, such as genetic engineering, or (ii) contain a new active substance indicated for the treatment of certain diseases.

Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of third-party reimbursement, which is time consuming and expensive. Reimbursement may not be available or sufficient to allow us to sell our future products, if any, on a competitive and profitable basis.

The passage of the Medicare Prescription Drug and Modernization Act of 2003 (the "MMA") imposed requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries, which may affect the marketing of our future products, if any. The MMA also introduced a reimbursement methodology, part of which went into effect in 2004, and a prescription drug plan, which went into effect on January 1, 2006. 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.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the E.U. 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. 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.

There have been and we expect that there will continue to be frequent federal and state proposals to impose governmental pricing controls or cost containment measures for prescription drugs. While we cannot predict whether such legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, contains provisions that may reduce the profitability of drugs, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Even if favorable coverage and reimbursement status is attained for one or more of our drug candidates for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Regulations

Pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, under certain conditions a sponsor may be granted marketing exclusivity for a period of five years following FDA approval. During this period, third parties would not be permitted to obtain FDA approval for a similar or identical drug through an Abbreviated NDA, which is the application form typically used by manufacturers seeking approval of a generic drug. The Hatch-Waxman Act also

permits a patent extension term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent extension cannot extend the remaining term of a patent beyond a total of 14 years. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus time of active FDA review between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and it must be applied for prior to expiration of the patent and within 60 days of the approval of the NDA.

In April 2015 and October 2016, prexigebersen received orphan drug designations for AML in the U.S. from the FDA and in the E.U. from the EMA, respectively. Orphan designation is available in the U.S. to drugs intended to treat, diagnose or prevent a rare disease or condition that affects fewer than 200,000 people in the U.S. at the time of application for orphan designation. Orphan drug designation must be requested before submitting an application for marketing authorization. Orphan designation qualifies the sponsor of the product for a tax credit and marketing incentives. The first sponsor to receive FDA marketing approval for a drug with an orphan designation is entitled to a seven-year exclusive marketing period in the U.S. for that product for that indication and, typically, a waiver of the prescription drug user fee for its marketing application. However, a drug that the FDA considers to be clinically superior to, or different from, the approved orphan drug, even though for the same indication, may also obtain approval in the U.S. during the seven-year exclusive marketing period. Orphan drug exclusive marketing rights may also 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 receive orphan drug designation from the EMA, a therapy must be intended for the treatment of a life-threatening or chronically debilitating rare condition with a prevalence of less than five in 10,000 in the E.U. Orphan drug designation provides incentives designed to facilitate development, including fee reductions for protocol assistance, scientific advice and importantly, may provide up to ten years of market exclusivity in the E.U. following product approval.

There is no guarantee that any of our other drug candidates will receive orphan drug designation or that, even if such drug candidate is granted such status, the drug candidate's clinical development and regulatory approval process will not be delayed or will be successful.

Pharmaceutical companies are also subject to various federal and state laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for any entity or person to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented, for payment to third party payors, including Medicare and Medicaid, claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

Company History and Available Information

The Company was incorporated in May 2000 as a Utah corporation. In February 2008, Bio-Path Subsidiary completed a reverse merger with the Company, which at the time was traded over the counter and had no current operations. The prior name of the Company was changed to Bio-Path Holdings, Inc. and the directors and officers of Bio-Path Subsidiary became the directors and officers of Bio-Path Holdings, Inc. On March 10, 2014, our common stock ceased trading on the OTCQX and commenced trading on the Nasdaq Capital Market under the ticker symbol "BPTH." Effective December 31, 2014, we changed our state of incorporation from Utah to Delaware through a statutory conversion pursuant to the Utah Revised Business Corporation Act and the Delaware General Corporation Law.

Our principal executive offices are located at 4710 Bellaire Boulevard, Suite 210, Bellaire, Texas 77401, and our telephone number is (832) 742-1357. Our Internet address is *www.biopathholdings.com*. We are not including the information contained in our website as part of, or incorporating it by reference into, this Annual Report on Form 10-K. We make available free of charge through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such materials with, or furnish it to, the SEC. We also make available on our website our Corporate Governance Guidelines; the charters for our Audit Committee, Nominating/Corporate Governance Committee and Compensation Committee; our Employee Code of Business Conduct and Ethics, which applies to all of our employees, including our executive officers; and our Code of Business Conduct and Ethics for Members of the Board of Directors. All such information is also available in print and free of charge to any of our stockholders who request it. In addition, we intend to disclose on our website any amendments to, or waivers from, our codes of business conduct and ethics that are required to be publicly disclosed pursuant to rules of the SEC.

ITEM 1A. RISK FACTORS

Risk Factor Summary

We are providing the following summary of the risk factors disclosed in this Annual Report on Form 10-K to enhance the readability and accessibility of our risk factor disclosures. We encourage our stockholders to carefully review the risk factors disclosed in this Form 10-K in their entirety for additional information regarding the material factors that make an investment in the Company speculative or risky.

- The COVID-19 pandemic could adversely impact our business, including our clinical trials.
- We are a clinical stage biotechnology company with no significant revenue. We have incurred significant operating losses since our inception, and we expect to incur losses for the foreseeable future and may never achieve profitability.
- We will continue to require substantial additional capital for the foreseeable future. If we are unable to raise additional capital when needed, we may be forced to delay, reduce or eliminate our drug development programs and commercialization efforts.
- The pharmaceutical and biotechnology industry is highly competitive. If we are unable to compete effectively, our drug candidates may be rendered noncompetitive or obsolete.
- Future collaboration arrangements to leverage our capabilities may not be successful.
- If we are unable to attract and retain key management, scientific personnel and advisors, we may not successfully develop our drug candidates or achieve our other business objectives.
- Our employees, agents, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with applicable regulatory standards and requirements.
- We expect to expand our operations, including clinical trials, in the future and may face challenges in managing our growth, which may result in disruptions to our operations.
- If we acquire or license technologies, resources or drug candidates, we will incur a variety of costs and may never realize benefits from the transaction.
- Our business has a substantial risk of product liability claims. If we are unable to obtain or maintain appropriate levels of insurance, a product liability claim could adversely affect our business.
- We are increasingly dependent on information technology systems to operate our business and a cyber-attack or other breach of our systems, or those of third parties on whom we may rely, could subject us to liability or interrupt the operation of our business.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- Provisions of our charter documents or Delaware law could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders, and could make it more difficult to change management.
- We face competition from entities that have developed or may develop therapeutic candidates for our target disease indications, including companies developing novel treatments and technology platforms based on modalities and technology that may be similar to ours. If these companies develop technologies, including delivery technologies, or therapeutic candidates more rapidly than we do, or their technologies are more effective, our ability to develop and successfully commercialize therapeutic candidates may be adversely affected.

- We may be subject, directly or indirectly, to certain U.S. federal and state healthcare laws and regulations, such as anti-kickback, false claims laws, physician payment transparency laws or similar fraud and abuse laws, which could expose us to potential criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

- Inadequate funding for the FDA, the SEC and other government agencies, or a work slowdown or stoppage at those agencies as part of a broader federal government shutdown, 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.

- We must complete extensive clinical trials to demonstrate the safety and efficacy of our drug candidates. If we are unable to demonstrate the safety and efficacy of our drug candidates, we will not be successful.

- Delays in the commencement of clinical trials of our drug candidates could result in increased costs to us and delay our ability to generate revenues.

- Delays in the completion of, or the termination of, clinical trials of our drug candidates could result in increased costs to us and could delay or prevent us from generating revenues.

- If we are unable to obtain U.S. and/or foreign regulatory approval, we will be unable to commercialize our drug candidates.

- In addition to regulations in the U.S., we may 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, if approved.

- Changes in existing laws and regulations affecting the healthcare industry could increase our costs and otherwise adversely affect our business.

- We rely on third parties to conduct clinical trials for our drug candidates, and their failure to timely and properly perform their obligations may result in costs and delays that prevent us from obtaining regulatory approval or successfully commercializing our drug candidates.

- We may not be able to obtain or maintain orphan drug exclusivity for our product candidates.

- We rely on third parties for manufacturing of our clinical drug supplies; our dependence on these manufacturers may impair the development of our drug candidates.

- There are underlying risks associated with the manufacture of our drug candidates, which have never been manufactured in large scale. Furthermore, we anticipate continued reliance on third-party manufacturers if we are successful in obtaining marketing approval from the FDA or other regulatory agencies for any of our drug candidates.

- Identification of previously unknown problems with respect to a drug candidate, manufacturer or facility may result in restrictions on the drug candidate, manufacturer or facility.

- We may experience delays in the development of our drug candidates if the third-party manufacturers of our drug candidates cannot meet FDA requirements relating to current Good Manufacturing Practices.

- If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our drug candidates, we may not generate product revenue.

- If our future drugs do not achieve market acceptance, we may be unable to generate significant revenue, if any.

- If third-party payors do not adequately reimburse patients for any of our drug candidates that are approved for marketing, they might not be purchased or used, and our revenues and profits will not develop or increase.

- If our patent position does not adequately protect our drug candidates, others could compete against us more directly, which would harm our business.

- If any third-party owners of intellectual property we may license in the future do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects will be harmed.

- If we infringe or are alleged to infringe intellectual property rights of third parties, our business could be harmed.

- Litigation regarding patents, intellectual property and other proprietary rights may be expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing drug candidates to market and harm our ability to operate.

- Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information and may not adequately protect our intellectual property.

- Raising additional capital may cause dilution to existing stockholders, restrict our operations or require us to relinquish rights. Additionally, sales of a substantial number of shares of our common stock or other securities in the public market could cause our stock price to fall.

- We may issue additional shares of our common stock in accordance with our equity incentive plans or upon exercise or conversion of outstanding securities that are exercisable for or convertible into shares of our common stock, which may cause dilution to existing stockholders.

- The trading price of our common stock has been volatile and is likely to be volatile in the future.

- Our common stock is thinly traded and in the future may continue to be thinly traded, and our stockholders may be unable to sell at or near asking prices or at all if they need to sell their shares to raise money or otherwise desire to liquidate such shares.

- Our certificate of incorporation grants our Board of Directors the power to designate and issue additional shares of common and/or preferred stock.

- We do not anticipate paying cash dividends, and accordingly stockholders must rely on stock appreciation for any return on their investment in us.

- Our management is required to devote substantial time and incur additional expense to comply with public company regulations.

- Failure to maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act of 2002 could have a material adverse effect on the price of our common stock.

- Our common stock may be delisted from The Nasdaq Capital Market which could negatively impact the price of our common stock and our ability to access the capital markets.

Risks Related to Our Business

The COVID-19 pandemic could adversely impact our business, including our clinical trials.

In December 2019, a novel strain of coronavirus, COVID-19, was reported to have surfaced in Wuhan, China. Since then, COVID-19 has evolved into a global pandemic, spreading to many countries, including the United States. Depending upon the severity of the COVID-19 outbreak, we may experience disruptions that could severely impact our business.

For instance, our clinical trials may be affected by the pandemic. Site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis may be paused or delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic. If COVID-19 continues to spread, some participants and clinical investigators may not be able to comply with clinical trial protocols. For example, quarantines or other travel limitations (whether voluntary or required) may impede participant movement, affect sponsor access to study sites, or interrupt healthcare services, and we may be unable to conduct our clinical trials. Additionally, infections and deaths related to the pandemic may disrupt the United States' healthcare and healthcare regulatory systems. Such disruptions could divert healthcare resources away from, or materially delay FDA review and/or approval of, our clinical trials. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

To date, COVID-19's impact on our operations has been limited to the inability to travel to clinical trial sites, clinical trial sites not allowing nonessential personnel on site for the purpose of monitoring activity and delays in the manufacture of our drug requirements by contracted third-party manufacturers. We anticipate COVID-19 may have an effect on patient recruiting in the near term as social distancing mandates are in effect. We believe these operational issues can be managed through remote monitoring capabilities currently being developed and deployed.

The global outbreak of COVID-19 continues to rapidly evolve. The extent to which COVID-19 may impact our business, including our clinical trials, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. We will continue to monitor the situation closely.

We are a clinical stage biotechnology company with no significant revenue. We have incurred significant operating losses since our inception, and we expect to incur losses for the foreseeable future and may never achieve profitability.

We have incurred significant operating losses since our inception. As of December 31, 2021, we had an accumulated deficit of $77.7 million. To date, we have not generated any revenue from the sale of our drug candidates and we do not expect to generate any revenue from sales of our drug candidates for the foreseeable future. We expect to continue to incur significant operating losses and we anticipate that our losses may increase substantially as we expand our drug development programs and commercialization efforts.

To achieve profitability, we must successfully develop and obtain regulatory approval for one or more of our drug candidates and effectively commercialize any drug candidates we develop. Even if we succeed in developing and commercializing one or more of our drug candidates, we may not be able to generate sufficient revenue and we may never be able to achieve or sustain profitability.

We will continue to require substantial additional capital for the foreseeable future. If we are unable to raise additional capital when needed, we may be forced to delay, reduce or eliminate our drug development programs and commercialization efforts.

We expect to continue to incur significant operating expenses in connection with our ongoing activities, including conducting clinical trials, manufacturing and seeking regulatory approval of our drug candidates, prexigebersen, prexigebersen-A, BP1002 and BP1003. In addition, if we obtain regulatory approval of one or more of our drug candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

As of December 31, 2021, we had $23.8 million in cash on hand, compared to $13.8 million as of December 31, 2020. Our ongoing future capital requirements will depend on numerous factors, including:

- the rate of progress, results and costs of completion of ongoing clinical trials of our drug candidates;
- the rate of progress, results and costs of completion of ongoing preclinical testing of our drug candidates;
- the size, scope, rate of progress, results and costs of completion of any potential future clinical trials and preclinical tests of our drug candidates that we may initiate;
- the costs to obtain adequate supply of the compounds necessary for our drug candidates;
- the costs of obtaining regulatory approval of our drug candidates;
- the scope, prioritization and number of drug development programs we pursue;
- the costs for preparing, filing, prosecuting, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other products and technologies and the costs to develop those products and technologies;
- the costs of future commercializing activities, including product sales, marketing, manufacturing and distribution, of any of our drug candidates or other products for which marketing approval has been obtained;
- our ability to establish strategic collaborations and licensing or other arrangements on terms favorable to us; and
- competing technological and market developments.

Any additional fundraising efforts may divert our management from their day to day activities, which may adversely affect our ability to develop and commercialize our drug candidates. Our ability to raise additional funds will depend, in part, on the success of our product development activities and other factors related to financial, economic and market conditions, many of which are beyond our control. There can be no assurance that we will be able to raise additional capital when needed or on terms that are favorable to us, if at all. If adequate funds are not available on a timely basis, we may be forced to:

- delay, reduce the scope of or eliminate one or more of our drug development programs;
- relinquish, license or otherwise dispose of rights to technologies, drug candidates or products that we would otherwise seek to develop or commercialize ourselves at an earlier stage or on terms that are less favorable than might otherwise be available; or
- liquidate and dissolve the Company.

If our operating plans change, we may require additional capital sooner than planned. Such additional financing may not be available when needed or on terms favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current and future operating plan.

The pharmaceutical and biotechnology industry is highly competitive. If we are unable to compete effectively, our drug candidates may be rendered noncompetitive or obsolete.

We are engaged in segments of the pharmaceutical and biotechnology industry that are highly competitive and characterized by rapid and significant technological change. Many large pharmaceutical and biotechnology companies, academic and research institutions, governmental agencies and other public and private research organizations are pursuing the development of novel drugs

that target AML, CML, ALL, MDS, lymphoma, ovarian, breast cancer, solid tumors and other cancers generally. We face, and expect to continue to face, intense and increasing competition as new products enter the market and advanced technologies become available. Our competitors may discover, develop or commercialize products or other novel technologies that are more effective, safer or less costly than our drug candidates. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for our drug candidates.

Many of our competitors have:

- significantly greater capital, technical and human resources than we have and may be better equipped to discover, develop, manufacture and commercialize drug candidates;
- more experience in drug discovery, development and commercialization, obtaining regulatory approvals and manufacturing and marketing pharmaceutical products;
- drug candidates that have been approved or are in late-stage clinical development; and/or
- collaboration arrangements in our target markets with leading companies and research institutions.

Mergers and acquisitions in the pharmaceutical and biotechnology industry 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, establishing clinical trial sites and patent registration for clinical trials, and acquiring technologies complementary to, or necessary for, our drug candidates and programs.

Competitive products and technological developments may render our drug candidates noncompetitive or obsolete before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and/or the widespread adoption or increased utilization of any vaccine for the diseases we are targeting could render our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for any of our drug candidates, we will face competition based on the safety and effectiveness of our drug candidates, the timing of their entry into the market in relation to competitive products in development, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent position and other factors. If we successfully develop drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful.

Future collaboration arrangements to leverage our capabilities may not be successful.

As part of our business strategy, we may enter into collaborative arrangements for the development and commercialization of our drug candidates. For our collaboration efforts to be successful, we must identify partners whose competencies complement ours. We must also successfully enter into collaboration agreements with them on terms attractive to us and integrate and coordinate their resources and capabilities with our own. We may be unsuccessful in entering into collaboration agreements with acceptable partners or negotiating favorable terms in these agreements. In addition, we may face a disadvantage in seeking to enter into or negotiating collaborations with potential partners because other potential collaborators may have greater management and financial resources than we do.

If we do enter into collaborative arrangements, the success of these collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Furthermore, we may face risks and uncertainties in connection with collaborative arrangements, including:

- inability to integrate the resources or capabilities of collaborators;
- collaborators may prove difficult to work with or less skilled than we originally expected;
- disputes may arise with respect to the ownership of rights to technology developed with collaborators;

- disagreements with collaborators could delay or terminate the research, development or commercialization of products or result in litigation or arbitration;

- difficulty enforcing our arrangements if one of our collaborators fails to perform;

- termination of our collaboration arrangements by collaborators, which could make it difficult for us to attract new collaborators or adversely affect the perception of us in the business or financial communities;

- collaborators may have considerable discretion in electing whether to pursue the development of any additional drug candidates and may pursue technologies or products either on their own or in collaboration with our competitors that are similar to or competitive with our technologies; and

- collaborators may change the focus of their development and commercialization efforts.

If we are unsuccessful in our collaborative efforts, our ability to develop and market drug candidates could be severely limited.

If we are unable to attract and retain key management, scientific personnel and advisors, we may not successfully develop our drug candidates or achieve our other business objectives.

Our success depends on the availability and contributions of members of our senior management team, scientific team and other key personnel. The loss of services of any of these individuals could delay, reduce or prevent our drug development and other business objectives. Furthermore, recruiting and retaining qualified scientific personnel to perform drug development work will be critical to our success. We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other public and private research institutions. We may be unable to attract and retain these individuals, and our failure to do so could materially adversely affect our business and financial condition.

Our employees, agents, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with applicable regulatory standards and requirements.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants, advisors and commercial partners. Misconduct by these persons could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the U.S. and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and cause serious harm to our business, financial condition and reputation. We currently have codes of business conduct and ethics applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and our codes of business conduct and ethics and the other precautions we take to detect and prevent improper activities may not be effective in controlling unknown or unmanaged risks or losses, or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of significant fines or other sanctions, which could materially adversely affect our business and financial condition. Whether or not we are successful in defending against such actions or investigations, we could incur substantial costs, including legal fees, and divert the attention of management in defending ourselves against any of these claims or investigations.

We expect to expand our operations, including clinical trials, in the future and may face challenges in managing our growth, which may result in disruptions to our operations.

We expect to expand our operations, including clinical trials for our drug candidates, over time. To successfully manage future growth, we may need to implement and improve our managerial, operational and financial resources, and may need to expand our facilities and recruit and train additional qualified personnel. Our expected growth may also require significant financial resources, which may not be available when needed or on terms favorable to us. Our senior management may be required to devote substantial

attention to managing growth activities and may be unable to effectively manage the expansion of our operations due to our limited resources, which may result in disruptions to our business operations and could harm our business and financial condition.

If we acquire or license technologies, resources or drug candidates, we will incur a variety of costs and may never realize benefits from the transaction.

If appropriate opportunities become available, we may license or acquire technologies, resources, drugs or drug candidates. We may never realize the anticipated benefits of such a transaction. In particular, due to the risks inherent in drug development, we may not successfully develop or obtain marketing approval for the drug candidates we acquire. Future licenses or acquisitions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, the creation of contingent liabilities, material impairment expenses related to goodwill and impairment or amortization expenses related to other intangible assets, which could harm our business and financial condition.

Our business has a substantial risk of product liability claims. If we are unable to obtain or maintain appropriate levels of insurance, a product liability claim could adversely affect our business.

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and sales and marketing of human therapeutic products. Although we do not currently commercialize any products, claims could be made against us based on the use of our drug candidates in clinical trials. Product liability claims could delay or prevent completion of our clinical development programs**.** We currently have product liability insurance, but we may not be able to maintain such insurance on acceptable terms. However, even if we maintain or obtain other product liability insurance, our insurance may not provide adequate coverage against potential liabilities. As a result, we may be unable to obtain or maintain insurance coverage at a reasonable cost to protect against losses that could harm our business and financial condition. If any claims are brought against us, and we are not successful in defending ourselves, those claims could result in damage awards against us, which could materially adversely affect our business and financial condition. Whether or not we are successful in defending against such claims, we could incur substantial costs, including legal fees, and divert the attention of management in defending ourselves against any of these claims.

We are increasingly dependent on information technology systems to operate our business and a cyber-attack or other breach of our systems, or those of third parties on whom we may rely, could subject us to liability or interrupt the operation of our business.

We are increasingly dependent on information technology systems to operate our business. A breakdown, invasion, corruption, destruction or interruption of critical information technology systems by employees, others with authorized access to our systems or unauthorized persons could negatively impact operations. In the ordinary course of business, we collect, store and transmit confidential information and it is critical that we do so in a secure manner to maintain the confidentiality and integrity of such information. Additionally, we outsource certain elements of our information technology systems to third parties. As a result of this outsourcing, our third party vendors may or could have access to our confidential information making such systems vulnerable. Data breaches of our information technology systems, or those of our third party vendors, may pose a risk that sensitive data may be exposed to unauthorized persons or to the public. For example, the loss of clinical trial data from completed or ongoing clinical trials or preclinical studies could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. While we believe that we have taken appropriate security measures to protect our data and information technology systems, and have been informed by our third party vendors that they have as well, there can be no assurance that our efforts will prevent breakdowns or breaches in our systems, or those of our third party vendors, that could materially adversely affect our business and financial condition.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), if a corporation experiences an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to utilize its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. Our prior and potential future equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change under Section 382 of the Code. If a limitation were to apply, utilization of a portion of our domestic net operating loss and tax credit carryforwards could be limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities.

On December 22, 2017, the U.S. government enacted legislation referred to as the Tax Cuts and Jobs Act (the "Tax Act"). Under the Tax Act, net operating losses generated prior to 2018 will continue to be governed by the net operating loss tax rules as they existed prior to the adoption of the new Tax Act, which means that generally they will expire 20 years after they were generated if not used prior thereto. Accordingly, our net operating losses could expire unused and be unavailable to offset future income tax liabilities, if any. Under the Tax Act, net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such net operating losses is limited to 80% of current year taxable income. We continue to examine the impact that this provision of the Tax Act, among other provisions, may have on our business.

Provisions of our charter documents or Delaware law could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders, and could make it more difficult to change management.

Provisions of our certificate of incorporation and bylaws may discourage, delay or prevent a merger, acquisition or other change in control that stockholders might otherwise consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. In addition, these provisions may frustrate or prevent any attempt by our stockholders to replace or remove our current management by making it more difficult to replace or remove our board of directors. These provisions include:

- limitations on our stockholders' ability to call special meetings of stockholders;
- an advance notice requirement for stockholder proposals and nominations for members of our Board;
- the authority of our Board to determine the number of director seats on our Board;
- the authority of our Board to fill vacancies occurring on the Board;
- the authority of our Board to issue preferred stock with such terms as our Board may determine.

In addition, because we are governed by Delaware law, we are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person who, together with its affiliates, owns or within the last three years has owned 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

We face competition from entities that have developed or may develop therapeutic candidates for our target disease indications, including companies developing novel treatments and technology platforms based on modalities and technology that may be similar to ours. If these companies develop technologies, including delivery technologies, or therapeutic candidates more rapidly than we do, or their technologies are more effective, our ability to develop and successfully commercialize therapeutic candidates may be adversely affected.

While we believe that our DNAbilize® technology is the only delivery method of its type, the area of cancer treatment research is rapidly progressing, with many stakeholders, including for-profit and nonprofit institutions, conducting preclinical and clinical studies of various types of therapeutic products for the same or similar indications for use as our drug candidates. We expect that such work by others will continue, which may make it difficult for us to effectively recruit and enroll a satisfactory number of participants in clinical trials.

Our success will partially depend on our ability to develop therapeutics that are safer and more effective than competing therapeutics. Our commercial opportunity and success will be reduced or eliminated if competing therapeutics are safer, more effective, or less expensive than the therapeutics we develop, or if any are granted exclusive marketing approval by the FDA that precludes the marketing of our drug candidates for a period of time. If our lead drug candidates are approved for the indications we are currently pursuing, they will compete with a range of therapeutic treatments that are either in development or currently marketed. For example, the FDA has recently approved a number of drugs indicated for treatment of AML, some of which may have target patient populations similar to that of our drug candidates.

Many of our competitors may have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain FDA approval for any drug candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered, the timing and scope of regulatory approvals (if we are able to obtain any) for these drug candidates, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing therapeutics could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any therapeutics we may develop. Competitive alternatives may make any drugs that we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our drug candidates, if we are able to obtain regulatory approval to commercialize such drug candidates.

We may be subject, directly or indirectly, to certain U.S. federal and state healthcare laws and regulations, such as anti-kickback, false claims laws, physician payment transparency laws or similar fraud and abuse laws, which could expose us to potential criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation, ordering and utilization of any products for which we obtain regulatory approval. If we obtain FDA approval for any of our products and begin commercializing those products in the U.S., our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician payment transparency laws and regulations. These laws may impact, among other things, our potential sales, marketing and education programs and our relationships with physicians, patients, and other persons or entities in a position to refer, use, or recommend our future products. The laws that may affect our ability to operate could include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which may be pursued through civil whistleblower or qui tam actions, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid or other third-party payors that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- federal criminal statutes under the Health Insurance Portability and Accountability Act of 1996, which 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, 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;

- the federal transparency requirements under The Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act (known collectively as the "Affordable Care Act"), including the provision commonly referred to as the Physician Payments Sunshine Act, which requires manufacturers of drugs, biologics, devices 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 information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- State law equivalents of each of the healthcare laws described above, some of which may be broader in scope and apply regardless of the type of payor, such as state anti-kickback statutes and false claims acts, and state pricing, marketing, and transparency statutes that require us to adopt compliance programs, report pricing information, or disclose payments or other transfers of value to physicians or other covered recipients.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws once our products are commercialized. In addition, healthcare reform legislation has strengthened these laws and additional laws or requirements may be implemented in the future. For example, the Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback and criminal healthcare fraud statutes. As a result of such amendment, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. Moreover, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Efforts to ensure that our business arrangements comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our existing or future business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Any such actions instituted against us could have a significant adverse impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Even if we are successful in defending against such actions, we may nonetheless be subject to substantial costs, reputational harm and adverse effects on our ability to operate our business.

If any of our employees, agents, or the physicians or other providers or entities with whom we expect to do business are found to have violated applicable laws, we may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, or, if we are not subject to such actions, we may suffer reputational harm for conducting business with persons or entities found, or accused of being, in violation of such laws. Any such events could adversely affect our ability to operate our business and our results of operations.

Inadequate funding for the FDA, the SEC and other government agencies, or a work slowdown or stoppage at those agencies as part of a broader federal government shutdown, 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 could adversely affect our business. For example, over the last several years, including December 22, 2018 to January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough employees and stop critical activities. If a prolonged government shutdown or a series of shutdowns occurs, it could significantly affect the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to gain access to the public markets and obtain necessary capital in order to properly capitalize and continue our operations, which could have a material adverse effect on our business and financial condition.

Risks Related to the Development of Our Drug Candidates

We must complete extensive clinical trials to demonstrate the safety and efficacy of our drug candidates. If we are unable to demonstrate the safety and efficacy of our drug candidates, we will not be successful.

To date, none of our drug candidates have been approved for sale in the U.S. or any foreign country. While antisense therapeutics have been in development for over 20 years, only a limited number of antisense drugs have been successfully developed to date. Further, the development of liposomal antisense therapeutics, which comprise our drug therapeutics technology, has faced

many challenges and generally remains unproven in the treatment of cancers. The success of our business depends primarily on our ability to develop and commercialize our drug candidates successfully. Our drug candidates must satisfy rigorous standards of safety and efficacy before they can be approved for sale. To satisfy these standards, we must engage in expensive and lengthy testing of our drug candidates.

We may not be able to obtain authority from the FDA or other equivalent foreign regulatory agencies to move on to further efficacy segments of our ongoing clinical trials or commence and complete any other clinical trials for any of our drug candidates. Positive results in preclinical studies of a drug candidate may not be predictive of similar results in human clinical trials, and promising results from early clinical trials of a drug candidate may not be replicated in later clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage development. Accordingly, the results from the preclinical tests or clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage trials. The failure of clinical trials to demonstrate safety and efficacy of one or more of our drug candidates will have a material adverse effect on our business and financial condition.

Delays in the commencement of clinical trials of our drug candidates could result in increased costs to us and delay our ability to generate revenues.

Our drug candidates will require continued extensive clinical trials prior to the submission of a regulatory application for commercial sales. Because of the nature of clinical trials, we do not know whether future planned clinical trials will begin on time, if at all. Delays in the commencement of clinical trials could significantly increase our drug development costs and delay any commercialization of our drug candidates. In addition, many of the factors that may cause, or lead to, a delay in the commencement of clinical trials may also ultimately lead to denial of regulatory approval of a drug candidate.

The commencement of clinical trials can be delayed for a variety of reasons, including delays in:

- demonstrating sufficient safety and efficacy in past clinical trials to obtain regulatory approval to commence a further clinical trial;
- convincing the FDA that we have selected valid endpoints for use in proposed clinical trials;
- reaching agreements on acceptable terms with prospective contract manufacturers for manufacturing sufficient quantities of our drug candidates; and
- obtaining institutional review board approval to conduct a clinical trial at a prospective site.

In addition, the commencement of clinical trials may be delayed due to insufficient patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

Delays in the completion of, or the termination of, clinical trials of our drug candidates could result in increased costs to us and could delay or prevent us from generating revenues.

Once a clinical trial has begun, it may be delayed, suspended or terminated by us or the FDA or other regulatory authorities due to a number of factors, including:

- regulators or institutional review boards may not authorize us to commence or conduct a clinical trial at a prospective trial site;
- our preclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical testing or clinical trials or we may abandon projects that we expect may not be promising;

- we might have to suspend or terminate our clinical trials if the participating patients are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;
- the cost of our clinical trials may be greater than we currently anticipate and we may lack adequate funding to continue the clinical trial;
- the timing of our clinical trials may be longer than we currently anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner (including delays or inability to manufacture or obtain sufficient quantities of materials for use in clinical trials);
- inadequacy of or changes in our manufacturing process or compound formulation;
- slower than expected rates of patient recruitment and enrollment or lower than expected patient retention rates;
- the effects of our drug candidates may not be the desired effects or may include undesirable side effects or our drug candidates may have other unexpected characteristics;
- changes in applicable regulatory policies and regulations;
- delays in identifying and reaching agreement on acceptable terms with prospective clinical trial sites;
- uncertainty regarding proper dosing;
- failure of our clinical research organizations to comply with all regulatory and contractual requirements or otherwise fail to perform their services in a timely or acceptable manner;
- scheduling conflicts with participating clinicians and clinical institutions;
- failure to construct appropriate clinical trial protocols;
- insufficient data to support regulatory approval;
- inability or unwillingness of medical investigators to follow our clinical protocols; and
- the timing of discussions and meetings with the FDA or other regulatory authorities regarding the scope or design of our clinical trials.

Many of these factors that may lead to a delay, suspension or termination of clinical trials of our drug candidates may also ultimately lead to denial of regulatory approval of our drug candidates.

From time to time, we may publicly announce our expected timing of completing certain milestones relating to various scientific, clinical, regulatory, development and other objectives related to our business. For example, these milestones may include the commencement or completion of scientific studies or clinical trials or the submission or approval of regulatory filings. Our estimates for completion of these milestones are based on a variety of assumptions, some of which may be out of our control.

If we experience delays in the completion of, or termination of, clinical trials of any drug candidates in the future, or if we do not meet our milestones within the estimated timeframes that we have publicly announced, our business, financial condition and the

commercial prospects for our drug candidates could be materially adversely affected, and our ability to generate product revenues could be delayed or eliminated. In addition, our stock price could decline.

If we are unable to obtain U.S. and/or foreign regulatory approval, we will be unable to commercialize our drug candidates.

Our drug candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, record keeping, labeling, marketing and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required in the U.S. and in many foreign jurisdictions prior to the commercial sale of our drug candidates. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the drug candidates we are developing will obtain marketing approval. In connection with the clinical trials for our drug candidates, we face risks that:

- the drug candidate may not prove to be efficacious;
- the drug candidate may not prove to be safe;
- the drug candidate may not be readily co-administered or combined with other drugs or drug candidates;
- the results may not confirm the positive results from earlier preclinical studies or clinical trials;
- the results may not meet the level of statistical significance required by the FDA or other regulatory agencies; and
- the FDA or other regulatory agencies may require us to carry out additional studies.

We have limited experience in conducting and managing later stage clinical trials necessary to obtain regulatory approvals, including approval by the FDA. However, this risk would be mitigated in the event the Company is successful entering into a co-development agreement with a pharma partner for late stage clinical development. The time required to complete clinical trials and for the FDA and other countries' regulatory review processes is uncertain and typically takes many years. Our analysis of data obtained from preclinical and clinical trials is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials, and FDA regulatory review.

Any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product and affect reimbursement by third-party payors. These limitations may limit the size of the market for the product. We may also become subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of foreign regulations. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. Foreign jurisdictions may have different approval procedures than those required by the FDA and may impose additional testing requirements for our drug candidates.

In addition to regulations in the U.S., we may 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, if approved.

Whether or not we obtain FDA approval for a drug candidate, we must obtain the requisite approvals from regulatory authorities in non-U.S. countries prior to the commencement of clinical trials or marketing of our products in those countries. Certain countries outside of the U.S. have a process that requires the submission of a clinical trial application, much like an IND, prior to the commencement of human clinical trials. In the E.U., for example, a CTA must be submitted to the competent national health authority and to independent ethics committees in each country in which a company intends to conduct clinical trials. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed in that country.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP and other applicable regulatory requirements.

To obtain regulatory approval of an investigational drug under E.U. regulatory systems, we must submit a marketing authorization application. This application is similar to the NDA in the U.S., with the exception of, among other things, country-specific document requirements. Drugs can be authorized in the E.U. by using (i) the centralized authorization procedure, (ii) the mutual recognition procedure, (iii) the decentralized procedure or (iv) national authorization procedures.

The EMA implemented the centralized procedure for the approval of human drugs to facilitate marketing authorizations that are valid throughout the E.U. This procedure results in a single marketing authorization granted by the European Commission that is valid across the E.U., as well as in Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for certain human drugs including those that are: (i) derived from biotechnology processes, such as genetic engineering, or (ii) contain a new active substance indicated for the treatment of certain diseases.

Changes in existing laws and regulations affecting the healthcare industry could increase our costs and otherwise adversely affect our business.

Our research and development activities, preclinical studies and clinical trials, and the manufacturing, marketing and labeling of any products we may develop, are subject to extensive regulation by the FDA and other regulatory authorities in the U.S. and other countries. Changes in existing federal, state and foreign laws and agency regulations may be established that could prevent or delay regulatory approval of our drug candidates or materially increase our costs, including:

- changes in the FDA and foreign regulatory processes for new therapeutics that may delay or prevent the approval of any of our drug candidates;
- new laws, regulations, or judicial decisions related to healthcare availability or the payment for healthcare products and services, including prescription drugs, that would make it more difficult for us to market and sell products once they are approved by the FDA or foreign regulatory agencies;
- changes in FDA and foreign regulations that may require additional safety monitoring prior to or after the introduction of new products to market, which could materially increase our costs of doing business; and
- changes in FDA and foreign current cGMP that would make it more difficult for us to manufacture our drug candidates in accordance with cGMP.

Delays in obtaining or preventing our obtaining regulatory approval of our drug candidates could materially adversely affect our ability to commercialize any of our drug candidates and our ability to receive product revenues or to receive milestone payments or royalties from any product rights we might license to others.

We rely on third parties to conduct clinical trials for our drug candidates, and their failure to timely and properly perform their obligations may result in costs and delays that prevent us from obtaining regulatory approval or successfully commercializing our drug candidates.

We rely on independent contractors, including clinical research organizations, in certain areas that are particularly relevant to our research and drug development plans, such as for data management for the conduct of clinical trials. The competition for these relationships is intense, and we may not be able to maintain our relationships with them on acceptable terms. Independent contractors generally may terminate their engagements at any time, subject to notice. As a result, we can control their activities only within certain limits, and they will devote only a certain amount of their time conducting research on and trials of our drug candidates and assisting in developing them. If they do not successfully carry out their duties under their agreements with us, fail to inform us if these trials fail to comply with clinical trial protocols or fail to meet expected deadlines, our clinical trials may need to be extended, delayed or terminated. We may not be able to enter into replacement arrangements without undue delays or excessive expenditures. If there are delays in testing or regulatory approvals as a result of the failure to perform by our independent contractors or other outside parties,

our drug candidate development costs will increase and we may not be able to attain regulatory approval for or successfully commercialize our drug candidates.

In addition, we have no control over the financial health of our independent contractors. Several of our independent contractors are in possession of valuable and sensitive information relating to the safety and efficacy of our drug candidates, and several others provide services to a significant percentage of the patients enrolled in our clinical trials in which such independent contractors participate. Should one or more of these independent contractors become insolvent, or otherwise are not able to continue to provide services to us, the clinical trial in which such contractor participates could become significantly delayed and we may be materially adversely affected as a result of the delays and additional expenses associated with such event.

We may not be able to obtain or maintain orphan drug exclusivity for our product candidates.

Prexigebersen has received orphan drug designations for the treatment of AML in the U.S. Orphan designation is available to drugs intended to treat, diagnose or prevent a rare disease or condition that affects fewer than 200,000 people in the U.S. at the time of application for orphan designation. Orphan drug designation must be requested before submitting an application for marketing authorization. Orphan designation qualifies the sponsor of the product for a tax credit and marketing incentives. The first sponsor to receive FDA marketing approval for a drug with an orphan designation is entitled to a seven-year exclusive marketing period in the U.S. for that product for that indication and, typically, a waiver of the prescription drug user fee for its marketing application. However, a drug that the FDA considers to be clinically superior to, or different from, the approved orphan drug, even though for the same indication, may also obtain approval in the U.S. during the seven-year exclusive marketing period. Orphan drug exclusive marketing rights may also 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.

In October 2016, prexigebersen also received orphan drug designation for AML in the E.U. from the EMA. To receive orphan drug designation from the EMA, a therapy must be intended for the treatment of a life-threatening or chronically debilitating rare condition with a prevalence of less than five in 10,000 in the E.U. Orphan drug designation provides incentives designed to facilitate development, including fee reductions for protocol assistance, scientific advice and importantly, may provide up to ten years of market exclusivity in the E.U. following product approval.

There is no guarantee that any of our other drug candidates will receive orphan drug designation or that, even if such drug candidate is granted such status, the drug candidate's clinical development and regulatory approval process will not be delayed or will be successful.

Risks Related to Manufacturing Our Drug Candidates

We rely on third parties for manufacturing of our clinical drug supplies; our dependence on these manufacturers may impair the development of our drug candidates.

We have no ability to internally manufacture the drug candidates that we need to conduct our clinical trials. For the foreseeable future, we expect to continue to rely on third-party manufacturers and other third parties to produce, package and store sufficient quantities of our drug candidates and any future drug candidates for use in our clinical trials. We have entered into agreements with third-party manufacturers for the manufacture of our drug requirements, including agreements for the manufacture of prexigebersen for use in our Phase 2 clinical trial in AML, as well as agreements for the manufacture of prexigebersen-A, BP1002 and BP1003 for use in our Phase 1 clinical trials. To date, we have made steady progress with our current third-party manufacturers, overcoming challenges associated with scaling up manufacturing to develop their capabilities to supply us with our necessary quantities of drug supplies for our clinical trials. However, we may face various risks and uncertainties in connection with our reliance on third-party manufacturers, including:

- reliance on third-party manufacturers for regulatory compliance and quality assurance;
- the possibility of breach of the manufacturing agreement by the third-party manufacturer because of factors beyond our control;

- the possibility of termination or nonrenewal of our manufacturing agreement by the third-party manufacturer at a time that is costly or inconvenient for us;

- the potential that third-party manufacturers will develop know-how owned by such third-party manufacturer in connection with the production of our drug candidates that is necessary for the manufacture of our drug candidates; and

- reliance on third-party manufacturers to assist us in preventing inadvertent disclosure or theft of our proprietary knowledge.

Our drug candidates are complicated and expensive to manufacture. If our third-party manufacturers fail to deliver our drug candidates for clinical use on a timely basis, with sufficient quality, and at commercially reasonable prices, we may be required to delay or suspend clinical trials or otherwise discontinue development of our drug candidates. While we may be able to identify replacement third-party manufacturers or develop our own manufacturing capabilities for these drug candidates, this process would likely cause a delay in the availability of our drug candidates and an increase in costs. In addition, third-party manufacturers may have a limited number of facilities in which our drug candidates can be manufactured, and any interruption of the operation of those facilities due to events such as equipment malfunction or failure or damage to the facility by natural disasters could result in the cancellation of shipments, loss of product in the manufacturing process or a shortfall in available drug candidates.

We may in the future elect to manufacture certain of our drug candidates in our own manufacturing facilities. If we do so, we will require substantial additional funds and need to recruit qualified personnel in order to build or lease and operate any manufacturing facilities.

There are underlying risks associated with the manufacture of our drug candidates, which have never been manufactured in large scale. Furthermore, we anticipate continued reliance on third-party manufacturers if we are successful in obtaining marketing approval from the FDA or other regulatory agencies for any of our drug candidates.

To date, our drug candidates have been manufactured in relatively small quantities for preclinical testing and clinical trials by third-party manufacturers, and have never been manufactured in large scale. Additionally, as in the development of any new compound, there are underlying risks associated with their manufacture. These risks include, but are not limited to, cost, process scale-up, process reproducibility, construction of a suitable process plant, timely availability of raw materials, as well as regulatory issues associated with the manufacture of an active pharmaceutical agent. Any of these risks may prevent us from successfully developing our drug candidates. Our failure, or the failure of our third-party manufacturers to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors and reliable product packaging for diverse environmental conditions, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could materially adversely affect our business and financial condition.

If the FDA or other regulatory agencies approve any of our drug candidates for commercial sale, we expect that we would continue to rely, at least initially, on third-party manufacturers to produce commercial quantities of such approved drug candidates. These manufacturers may not be able to successfully increase the manufacturing capacity for any of our approved drug candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA or other regulatory authorities must review and approve. If our third-party manufacturers are unable to successfully increase the manufacturing capacity for a drug candidate, or we are unable to establish our own manufacturing capabilities, the commercial launch of any approved products may be delayed or there may be a shortage in supply.

Identification of previously unknown problems with respect to a drug candidate, manufacturer or facility may result in restrictions on the drug candidate, manufacturer or facility.

The FDA stringently applies regulatory standards for the manufacturing of our drug candidates. Identification of previously unknown problems with respect to a drug candidate, manufacturer or facility may result in restrictions on the drug candidate, manufacturer or facility, including warning letters, suspensions of regulatory approvals, operating restrictions, delays in obtaining new product approvals, withdrawal of the product from the market, product recalls, fines, injunctions and criminal prosecution. Any of the foregoing could have a material adverse effect on our business and financial condition.

We may experience delays in the development of our drug candidates if the third-party manufacturers of our drug candidates cannot meet FDA requirements relating to current Good Manufacturing Practices.

Our third-party manufacturers are required to produce our drug candidates under FDA cGMP in order to meet acceptable standards for our preclinical testing and clinical trials. If such standards change, the ability of third-party manufacturers to produce our drug candidates on the schedule we require for our preclinical tests and clinical trials may be affected. In addition, third-party manufacturers may not perform their obligations under their agreements with us or may discontinue their business before the time required by us to gain approval for or commercialize our drug candidates. Any difficulties or delays in the manufacturing and supply of our drug candidates could increase our costs or cause us to lose revenue or postpone or cancel clinical trials.

The FDA also requires that we demonstrate structural and functional comparability of a drug candidate produced by different third-party manufacturers. Because we may use multiple sources to manufacture our drug candidates, we may need to conduct comparability studies to assess whether manufacturing changes have affected the safety, identity, purity or potency of any drug candidate compared to the drug candidate produced by another manufacturer. If we are unable to demonstrate comparability, the FDA could require us to conduct additional clinical trials, which would be expensive and significantly delay commercialization of our drug candidates.

Risks Related to Commercialization

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our drug candidates, we may not generate product revenue.

We have no commercial products, and we do not currently have an organization for the sales and marketing of pharmaceutical products. In order to successfully commercialize any drug candidates that may be approved in the future by the FDA or comparable foreign regulatory authorities, we must build our sales and marketing capabilities or make arrangements with third parties to perform these services. For certain drug candidates in selected indications where we believe that an approved product could be commercialized by a specialty sales force that calls on a limited but focused group of physicians, we may commercialize these products ourselves. However, in therapeutic indications that require a large sales force selling to a large and diverse prescribing population, we may enter into arrangements with other companies for commercialization. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable.

If our future drugs do not achieve market acceptance, we may be unable to generate significant revenue, if any.

Even if our drug candidates obtain regulatory approval, they may not gain market acceptance among physicians, health care payors, patients and the medical community. Factors that we believe could materially affect market acceptance of our drug candidates include:

- the timing of market introduction of competitive drugs;
- the demonstrated clinical safety and efficacy of our drug candidates compared to other drugs and other drug candidates;
- the suitability of our drug candidates to be co-administered or combined with other drugs or drug candidates;
- the durability of our drug candidates in their ability to prevent the emergence of drug-resistant viral mutants;
- the convenience and ease of administration of our drug candidates;
- the existence, prevalence and severity of adverse side effects;
- other potential advantages of alternative treatment methods;

- the effectiveness of marketing and distribution support;
- the cost-effectiveness of our drug candidates; and
- the availability of reimbursement from managed care plans, the government and other third-party payors.

If our approved drug candidates fail to achieve market acceptance, we would not be able to generate significant revenue. In addition, even if our approved drug candidates achieve market acceptance, we may not be able to maintain that market acceptance over time if:

- new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete;
- unforeseen complications arise with respect to the use of our products; or
- sufficient third-party insurance coverage or reimbursement does not remain available.

If third-party payors do not adequately reimburse patients for any of our drug candidates that are approved for marketing, they might not be purchased or used, and our revenues and profits will not develop or increase.

Our revenues and profits will depend significantly upon the availability of adequate reimbursement for the use of any approved drug candidates from governmental and other third-party payors, both in the U.S. and in foreign markets. Reimbursement by a third party may depend upon a number of factors, including the third-party payor's determination that use of an approved drug candidate 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.

The regulations that govern marketing approvals, pricing and reimbursement for new therapeutic and diagnostic products vary widely from country to country. Some countries require approval of the sale price of a drug candidate before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the approved drug and negatively impact the revenues we are able to generate from the sale of the approved drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain regulatory approval.

Obtaining reimbursement approval for an approved drug from each third-party and government payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of any approved drug candidates to each payor. We may not be able to provide data sufficient to gain acceptance with respect to reimbursement. There also exists substantial uncertainty concerning third-party reimbursement for the use of any approved drug incorporating new technology, and even if determined eligible, coverage may be more limited than the purposes for which the drug is approved by the FDA. Moreover, eligibility for coverage does not imply that any approved drug will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Interim payments for new products, if applicable, may also be insufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the approved drugs and the clinical setting in which it is used, may be based on payments allowed for lower-cost products or combinations of products that are

already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or imperfections in Medicare or Medicaid data used to calculate these rates. Net prices for products may be reduced by mandatory discounts or rebates required by government health care programs or by any future relaxation of laws that restrict imports of certain medical products from countries where they may be sold at lower prices than in the U.S.

In the U.S., at both the federal and state levels, the government regularly proposes legislation to reform health care and its cost, and such proposals have received increasing political attention. While health care reform may increase the number of patients who have insurance coverage for the use of any approved drug, it may also include changes that adversely affect reimbursement for approved drugs. In addition, there has been, and we expect that there will continue to be, federal and state proposals to constrain expenditures for medical products and services, which may affect payments for any of our drug candidates that obtain approval. The Centers for Medicare and Medicaid Services frequently change product descriptors, coverage policies, product and service codes, payment methodologies and reimbursement values. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates and may have sufficient market power to demand significant price reductions. As a result of actions by these third-party payors, the health care industry is experiencing a trend toward containing or reducing costs through various means, including lowering reimbursement rates, limiting therapeutic class coverage and negotiating reduced payment schedules with service providers for drug products.

Our inability to promptly obtain coverage and profitable reimbursement rates from government-funded and private payors for any of our drug candidates that obtain approval could have a material adverse effect on our business and financial condition.

Risks Related to Intellectual Property

If our patent position does not adequately protect our drug candidates, others could compete against us more directly, which would harm our business.

Our patent portfolio currently includes five issued patents in the U.S. and two issued patents in foreign jurisdictions:

Claims Related to DNAbilize®

Patent No.	Title	Date Issued
US 9,744,187	P-ethoxy nucleic acids for liposomal formulation	August 29, 2017
US 10,335,428	P-ethoxy nucleic acids for liposomal formulation	July 2, 2019
US 10,898,506	P-ethoxy nucleic acids for liposomal formulation	January 26, 2021
SG 11201802718P	P-ethoxy nucleic acids for liposomal formulation	May 12, 2021
EA 038277	P-ethoxy nucleic acids for liposomal formulation	August 4, 2021

Compositions and Methods of Use for Specific Drug Targets

Patent No.	Title	Date Issued
US 10,927,379	Combination therapy with liposomal antisense oligonucleotides	February 23, 2021
US 11,041,153	P-ethoxy nucleic acids for STAT3 inhibition	June 22, 2021

We have six additional pending patent applications in the U.S. In addition, we have pending patent applications in key foreign jurisdictions across our six families of applications. Our success depends in large part on our ability to obtain and maintain patent protection both in the U.S. and in other countries for our drug candidates. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to maintain, obtain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any issued patents may not provide us with sufficient

protection for our drug candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us.

Even if patents have issued or will issue, we cannot guarantee that the claims of these patents are or will be valid or enforceable or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us. Patent applications in the U.S. are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the USPTO for the entire time prior to issuance as a U.S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we or our licensors were the first to invent, or the first to file patent applications on, our drug candidates. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a loss of our U.S. patent position. Furthermore, we may not have identified all U.S. and foreign patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies that affect our drug market.

The claims of the issued patents that are licensed to us, and the claims of any patents which may issue in the future and be owned by or licensed to us, may not confer on us significant commercial protection against competing products. Additionally, our patents may be challenged by third parties, resulting in the patent being deemed invalid, unenforceable or narrowed in scope, or the third party may circumvent any such issued patents. Our patents might not contain claims that are sufficiently broad to prevent others from utilizing our technologies. Consequently, our competitors may independently develop competing products that do not infringe our patents or other intellectual property. To the extent a competitor can develop similar products using a different molecule, our patents may not prevent others from directly competing with us.

The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the U.S. and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed.

Because of the extensive time required for development, testing and regulatory review of a drug candidate, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization of our drug candidates, thereby reducing any advantages of the patent. To the extent our drug candidates based on that technology are not commercialized significantly ahead of the date of any applicable patent, or to the extent we have no other patent protection on such drug candidates, those drug candidates would not be protected by patents, and we would then rely solely on other forms of exclusivity, such as regulatory exclusivity provided by the FDCA or trade secret protection.

The Leahy-Smith America Invents Act (the "America Invents Act") was signed into law in September 2011, and many of the substantive changes became effective in March 2013. The America Invents Act reforms U.S. patent law in part by changing the standard for patent approval from a "first to invent" standard to a "first to file" standard and developing a post-grant review system. This legislation changes U.S. patent law in a way that may weaken our ability to obtain patent protection in the U.S. for those applications filed after March 2013.

If any third-party owners of intellectual property we may license in the future do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects will be harmed.

We may enter into licenses for third-party intellectual property in the future. Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for their intellectual property, in particular, those patents to which we have secured exclusive rights. If applicable, our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents issue in respect of any such patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. In addition, our licensors may terminate their agreements with us in the event we breach the applicable license agreement and fail to cure the breach within a specified period of time. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could materially adversely affect our competitive business position, business prospects and financial condition.

Because our research and development of drug candidates incorporates compounds and other information that is the intellectual property of third parties, we depend on continued access to such intellectual property to conduct and complete our

preclinical and clinical research and commercialize the drug candidates that result from this research. We expect that future licenses would impose, numerous obligations on us. For example, under our existing and future license agreements, we may be required to pay (i) annual maintenance fees until a drug candidate is sold for the first time, (ii) running royalties on net sales of drug candidates, (iii) minimum annual royalties after a drug candidate is sold for the first time, and (iv) one-time payments upon the achievement of specified milestones. We may also be required to reimburse patent costs incurred by the licensor, or we may be obligated to pay additional royalties, at specified rates, based on net sales of our drug candidates that incorporate the licensed intellectual property rights. We may also be obligated under some of these agreements to pay a percentage of any future sublicensing revenues that we may receive. Future license agreements may also include payment obligations such as milestone payments or minimum expenditures for research and development. We expect that any future licenses would contain reporting, insurance and indemnification requirements.

If we infringe or are alleged to infringe intellectual property rights of third parties, our business could be harmed.

Our research, development and commercialization activities, including any drug candidates resulting from these activities, may infringe or be claimed to infringe patents or other proprietary rights owned by third parties and to which we do not hold licenses or other rights. There may be applications that have been filed but not published that, if issued, could be asserted against us. If a patent infringement suit were brought against us, we could be forced to stop or delay research, development or manufacturing of drug candidate that is the subject of the suit. Further, if we are found to have infringed a third- party patent, we could be obligated to pay royalties and/or other payments to the third party related to our drug candidates, which may be substantial, or we could be enjoined from selling our drug candidates that obtain approval.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition to infringement claims against us, we may become a party to other patent litigation and other proceedings, including interference proceedings declared by the USPTO and opposition proceedings in the European Patent Office, regarding intellectual property rights with respect to our drug candidates and technology. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business and financial condition.

Litigation regarding patents, intellectual property and other proprietary rights may be expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing drug candidates to market and harm our ability to operate.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Although we are not currently aware of any litigation or other proceedings or third-party claims of intellectual property infringement related to our drug candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may obtain patents in the future and allege that the use of our technologies infringes these patent claims or that we are employing their proprietary technology without authorization. Likewise, third parties may challenge or infringe upon our existing or future patents. Proceedings involving our patents or patent applications or those of others could result in adverse decisions regarding:

- the patentability of our inventions relating to our drug candidates; and/or
- the enforceability, validity or scope of protection offered by our patents relating to our drug candidates.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may:

- incur substantial monetary damages;
- encounter significant delays in bringing our drug candidates to market; and/or

- be precluded from participating in the manufacture, use or sale of our drug candidates or methods of treatment requiring licenses.

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, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information and may not adequately protect our intellectual property.

We rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. In order to protect our proprietary technology and processes, we also rely in part on confidentiality and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information nor result in the effective assignment to us of intellectual property, and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information or other breaches of the agreements. In addition, others may independently discover our trade secrets and proprietary information, and in such case we could not assert any trade secret rights against such party. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the U.S. may be less willing to protect trade secrets. Costly and time-consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could materially adversely affect our business and financial condition.

Risks Related to Our Securities

Raising additional capital may cause dilution to existing stockholders, restrict our operations or require us to relinquish rights. Additionally, sales of a substantial number of shares of our common stock or other securities in the public market could cause our stock price to fall.

We expect to seek the additional capital necessary to fund our operations through public or private equity offerings, collaboration agreements, debt financings or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, existing stockholders' ownership interests will be diluted and the terms may include liquidation or other preferences that adversely affect their rights as a stockholder. Debt financing, if available, may involve agreements that include 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 funds through collaboration or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or drug candidates, or grant licenses on terms that are not favorable to us. In addition, sales of a substantial number of shares of our common stock or other securities in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

We may issue additional shares of our common stock in accordance with our equity incentive plans or upon exercise or conversion of outstanding securities that are exercisable for or convertible into shares of our common stock, which may cause dilution to existing stockholders.

As of December 31, 2021, there were 485,908 shares of common stock reserved for issuance upon the exercise of outstanding options granted under our equity incentive plans. As of December 31, 2021, there were 190,224 additional shares of common stock reserved for future issuance of awards under the Bio-Path Holdings, Inc. 2017 Stock Incentive Plan, as amended (the "2017 Stock Incentive Plan"). In addition, as of December 31, 2021, there were 429,791 shares of common stock reserved for issuance upon the exercise of outstanding warrants that we have issued in connection with prior securities offerings. To the extent that outstanding stock options and warrants are exercised, existing stockholders' ownership interests may be diluted, which may reduce the market price of our common stock.

The trading price of our common stock has been volatile and is likely to be volatile in the future.

The trading price of our common stock has been highly volatile. On March 10, 2014, our common stock commenced trading on The Nasdaq Capital Market, and there is a limited history on which to gauge the volatility of our stock price on The Nasdaq Capital Market. From January 1, 2019 through December 31, 2021, our stock price has fluctuated from a low of $1.84 to a high of $73.52, after adjustment for reverse stock splits. The market price for our common stock will be affected by a number of factors, including:

- the denial or delay of regulatory approvals of our drug candidates or receipt of regulatory approval of competing products;
- our ability to accomplish clinical, regulatory and other drug development milestones;
- the ability of our drug candidates, if they receive regulatory approval, to achieve market success;
- the performance of third-party manufacturers and suppliers;
- developments with respect to patents and other intellectual property rights;
- sales of common stock or other securities by us or our stockholders in the future;
- additions or departures of key scientific or management personnel;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our drug candidates;
- trading volume of our common stock;
- investor perceptions about us and our industry;
- public reaction to our press releases, other public announcements and SEC and other filings;
- the failure of analysts to cover us, or changes in analysts' estimates or recommendations;
- the failure by us to meet analysts' projections or guidance;
- general market conditions and other factors unrelated to our operating performance or the operating performance of our competitors; and
- the other factors described elsewhere in this "Item 1A. Risk Factors" or the section titled "Risk Factors" contained in our other public filings.

The stock prices of many companies in the biotechnology industry have experienced wide fluctuations that have often been unrelated to the operating performance of these companies. Following periods of volatility in the market price of a company's securities, securities class action litigation often has been initiated against a company. If any class action litigation is initiated against us, we may incur substantial costs and our management's attention may be diverted from our operations, which could materially adversely affect our business and financial condition.

Our common stock is thinly traded and in the future may continue to be thinly traded, and our stockholders may be unable to sell at or near asking prices or at all if they need to sell their shares to raise money or otherwise desire to liquidate such shares.

To date, we have a low volume of daily trades in our common stock on The Nasdaq Capital Market. Our stockholders may be unable to sell their common stock at or near their asking prices or at all, which may result in substantial losses to our stockholders.

The market for our common stock may be characterized by significant price volatility when compared to seasoned issuers, and we expect that our share price will be more volatile than a seasoned issuer for the foreseeable future. As noted above, our common stock may be sporadically and/or thinly traded. As a consequence of this lack of liquidity, the trading of relatively small quantities of shares by our stockholders may disproportionately influence the price of those shares in either direction.

Our certificate of incorporation grants our Board of Directors the power to designate and issue additional shares of common and/or preferred stock.

Our authorized capital consists of 200,000,000 shares of common stock and 10,000,000 shares of preferred stock. Our preferred stock may be designated into series pursuant to authority granted by our certificate of incorporation, and on approval from our Board of Directors (the "Board"). The Board, without any action by our stockholders, may designate and issue shares in such classes or series as the Board deems appropriate and establish the rights, preferences and privileges of such shares, including dividends, liquidation and voting rights. The rights of holders of other classes or series of stock that may be issued could be superior to the rights of holders of our common shares. The designation and issuance of shares of capital stock having preferential rights could adversely affect other rights appurtenant to shares of our common stock.

We do not anticipate paying cash dividends, and accordingly stockholders must rely on stock appreciation for any return on their investment in us.

We anticipate that we will retain our earnings, if any, for future growth and therefore do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our common stock will provide a return to stockholders.

Our management is required to devote substantial time and incur additional expense to comply with public company regulations.

As a public reporting company, we are subject to the Sarbanes-Oxley Act of 2002, as well as to the information and reporting requirements of the SEC and other federal securities laws. We are also subject to the rules of The Nasdaq Stock Market. As a result, we incur significant legal, accounting, and other expenses that we would not incur as a private company, including costs associated with our public company reporting requirements and corporate governance requirements. Compliance with these public company obligations places significant additional demands on our limited number of finance and accounting staff and on our financial, accounting and information systems.

Failure to maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act of 2002 could have a material adverse effect on the price of our common stock.

Section 404 of the Sarbanes-Oxley Act of 2002 and the related rules and regulations of the SEC require an annual management assessment of the effectiveness of our internal control over financial reporting. As a smaller reporting company as defined in Rule 12b-2 under the Exchange Act, we are currently exempt from the auditor attestation requirement of Section 404(b). If we lose this eligibility, we will incur increased personnel and audit fees in connection with the additional audit requirements. If we fail to maintain the adequacy of our internal control over financial reporting, we may not be able to ensure that we can conclude on an ongoing basis that we have effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act of 2002 and the related rules and regulations of the SEC. If we cannot in the future favorably assess the effectiveness of our internal control over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on the price of our common stock.

Our common stock may be delisted from The Nasdaq Capital Market which could negatively impact the price of our common stock and our ability to access the capital markets.

The listing standards of The Nasdaq Capital Market provide that a company, in order to qualify for continued listing, must maintain (1) a board of directors comprised of a majority of Independent Directors (as defined in Nasdaq Listing Rule 5605(a)(2)) and an audit committee of the board of directors comprised of at least three members, each of whom must be an Independent Director, and (2) a minimum stock price of $1.00 and satisfy standards relative to minimum stockholders' equity, minimum market value of publicly held shares and various additional requirements.

If we fail to comply with all listing standards applicable to issuers listed on The Nasdaq Capital Market, our common stock may be delisted. If our common stock is delisted, it could reduce the price of our common stock and the levels of liquidity available to our stockholders. In addition, the delisting of our common stock could materially adversely affect our access to the capital markets and any limitation on liquidity or reduction in the price of our common stock could materially adversely affect our ability to raise capital. Delisting from The Nasdaq Capital Market could also result in other negative consequences, including the potential loss of confidence by suppliers, customers and employees, the loss of institutional investor interest and fewer business development opportunities.

As previously reported, due solely to the resignation of Martina Molsbergen from her position as a member of the Board and all committees of the Board on which she served (the "Director Resignation") as described in the Company's Current Report on Form 8-K filed on February 18, 2022, the Company is not in compliance with the continued listing requirements as set forth in Nasdaq Listing Rules 5605(b)(1) and 5605(c)(2)(A) regarding the composition of the Board and the Audit Committee (as hereinafter defined), respectively, because a majority of the Board is not comprised of Independent Directors and the Audit Committee is not comprised of three Independent Directors. Also as previously reported, the Listing Qualifications Department of Nasdaq has granted the Company a cure period to regain compliance with such Nasdaq Listing Rules, which cure period will expire upon the earlier of the Company's next annual stockholders' meeting or February 14, 2023; provided, however, that if the Company's next annual stockholders' meeting occurs no later than 180 days following the Director Resignation, then the cure period will expire 180 days following the Director Resignation. The Board intends to appoint a new Independent Director to fill the vacancy prior to the expiration of such cure period in order to regain compliance with such Nasdaq Listing Rules, but there can be no assurance that the Board will be able to do so.

In the past, we have received a notice of non-compliance from the Listing Qualifications Department of The Nasdaq Stock Market LLC with respect to the $1.00 minimum closing bid price requirement. Although we have regained compliance with the minimum closing bid price requirement after implementing reverse stock splits, there can be no assurance that we will be able to meet the minimum closing bid price requirement or other listing requirements in the future.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

In April 2014, we entered into a lease agreement for approximately 3,000 square feet of office space for general and administrative purposes in Bellaire, Texas, which is part of the Houston metropolitan area. The term of the lease began on August 1, 2014 and was scheduled to terminate on July 31, 2019. In May 2019, we entered into an amendment to the lease agreement to extend the term of the lease to October 31, 2024.

In April 2016, we entered into a lease agreement for approximately 2,100 square feet of lab space located in Bellaire, Texas for research and development purposes. The term of the lease began on May 1, 2016 and was scheduled to terminate on April 30, 2019. In December 2018, we entered into an amendment to the lease agreement to extend the term of the lease to April 30, 2022. In January 2022, we exercised an option in the lease agreement amendment to extend the term of the lease to April 30, 2025.

We do not own or lease any other real property that is materially important to our business. We believe that our current facilities are adequate for our current needs and that additional space will be available when and as needed.

ITEM 3. LEGAL PROCEEDINGS

None.

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

Our common stock is listed on The Nasdaq Capital Market under the symbol "BPTH."

Holders

As of March 3, 2022, there were 7,160,164 shares of our common stock outstanding and approximately 196 stockholders of record.

Dividends

We have not paid any cash dividends since our inception and do not anticipate or contemplate paying dividends in the foreseeable future.

Unregistered Sales of Equity Securities and Use of Proceeds

None.

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

In addition to historical information, this Annual Report on Form 10-K contains forward-looking statements that involve significant risks and uncertainties, which may cause our actual results to differ materially from plans and results discussed in forward-looking statements. We encourage you to review the risks and uncertainties, discussed in "Item 1A. Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements," included elsewhere in this Annual Report on Form 10-K. The risks and uncertainties can cause actual results to differ significantly from those forecasted in forward-looking statements or implied in historical results and trends.

The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

Overview

We are a clinical and preclinical stage oncology focused RNAi nanoparticle drug development company utilizing a novel technology that achieves systemic delivery for target specific protein inhibition for any gene product that is over-expressed in disease. Our drug delivery and antisense technology, called DNAbilize®, is a platform that uses P-ethoxy, which is a DNA backbone modification that is intended to protect the DNA from destruction by the body's enzymes when circulating in vivo, incorporated inside of a lipid bilayer having neutral charge. We believe this combination allows for high efficiency loading of antisense DNA into non-toxic, cell-membrane-like structures for delivery of the antisense drug substance into cells. In vivo, the DNAbilize® delivered antisense drug substances are systemically distributed throughout the body to allow for reduction or elimination of target proteins in blood diseases and solid tumors. Through testing in numerous animal studies and treatment in over 80 patients, our DNAbilize® drug candidates have demonstrated an excellent safety profile. DNAbilize® is a registered trademark of the Company.

Using DNAbilize® as a platform for drug development and manufacturing, we currently have four drug candidates in development to treat at least five different cancer disease indications. Our lead drug candidate, prexigebersen (pronounced prex" i je

ber' sen), which targets growth factor receptor-bound protein 2 (Grb2), initially started the efficacy portion of a Phase 2 clinical trial for untreated AML patients in combination with LDAC. The interim data released on March 6, 2019 showed that 11 (65%) of the 17 evaluable patients had a response, including five (29%) who achieved CR, including one CRi and one morphologic leukemia free state, and six (35%) stable disease responses, including two patients who had greater than a 50% reduction in bone marrow blasts. However, DNA hypomethylating agents are now the most frequently used agents in the treatment of elderly AML patients in the U.S. and Europe. As a result, Stage 2 of the Phase 2 trial in AML was amended to remove the combination treatment of prexigebersen and LDAC and replace it with the combination treatment of prexigebersen and decitabine, a DNA hypomethylating agent, for treatment of a second cohort of untreated AML patients. Since decitabine is also used as a treatment for relapsed/refractory AML patients, a cohort of relapsed/refractory AML patients was also added to the study.

The FDA granted approval of venetoclax in combination with LDAC, decitabine or azacytidine (the latter two drugs are DNA hypomethylating agents) as frontline therapy for newly diagnosed AML in adults who are 75 years or older, or who have comorbidities precluding intensive induction chemotherapy. We believe this approval of the frontline venetoclax and decitabine combination therapy provides an opportunity for combining prexigebersen with the combination therapy for the treatment of *de novo* AML patients. Preclinical efficacy studies for the triple combination treatment of prexigebersen, decitabine and venetoclax in AML have been successfully completed. In the preclinical efficacy studies, four AML cancer cell lines were treated with three different combinations of decitabine, venetoclax and prexigebersen. Decrease in AML cell viability was the primary measure of efficacy. The triple combination of decitabine, venetoclax and prexigebersen showed significant improvement in efficacy in three of the four AML cell lines. Based on these results, we believe that adding prexigebersen to the treatment combination of decitabine and venetoclax could lead to improved efficacy in AML patients. Accordingly, we further amended Stage 2 of this Phase 2 clinical trial to add the triple combination treatment comprised of prexigebersen, decitabine and venetoclax.

Bio-Path's approved amended Stage 2 for this Phase 2 clinical trial currently has three cohorts of patients. The first two cohorts will treat patients with the triple combination of prexigebersen, decitabine and venetoclax. The first cohort will include untreated AML patients, and the second cohort will include relapsed/refractory AML patients. Finally, the third cohort will treat relapsed/refractory AML patients, who are venetoclax-resistant or -intolerant, with the two-drug combination of prexigebersen and decitabine. The full trial design plans have approximately 98 evaluable patients for the first cohort having untreated AML patients with a preliminary review performed after 19 evaluable patients and a formal interim analysis after 38 evaluable patients. The full trial design plans have approximately 54 evaluable patients for each of the second cohort, having relapsed/refractory AML patients, and the third cohort, having AML patients who are venetoclax-resistant or -intolerant, in each case with a review performed after 19 evaluable patients. The study is anticipated to be conducted at ten clinical sites in the U.S., and Gail J. Roboz, MD is the national coordinating Principal Investigator for the Phase 2 trial. Dr. Roboz is a professor of medicine and director of the Clinical and Translational Leukemia Program at the Weill Medical College and the New York-Presbyterian Hospital in New York City. On August 13, 2020, we announced the enrollment and dosing of the first patient in this approved amended Stage 2 of the Phase 2 clinical trial.

On April 5, 2021, we announced the successful completion of the safety run-in of Stage 2 of the Phase 2 clinical study. In the safety run-in of the triple combination, six evaluable patients were treated with the combination of prexigebersen, decitabine and venetoclax. These patients included four relapsed/refractory AML patients, and two newly diagnosed AML patients. In the preliminary safety data review, five of the patients (83%) responded to treatment, including four (67%) achieving CR and one (17%) achieving CRi. Recent publications provide that CR rates to combination treatment with decitabine and venetoclax (but without prexigebersen) are 42 to 52% for relapsed/refractory AML patients and 0 to 39% for relapsed/refractory secondary AML patients. Response rates to frontline treatment with decitabine and venetoclax (but without prexigebersen) are 62 to 71% for newly diagnosed AML patients. These preliminary data, presented at the 2021 American Society of Hematology Annual Meeting, showed the treatment was well-tolerated and there were no dose limiting toxicities attributed to prexigebersen. Three patients remained on treatment for more than one cycle.

In addition, a modified product named prexigebersen-A, Bio-Path's fourth drug candidate, has shown to enhance chemotherapy efficacy in preclinical solid tumor models. Prexigebersen-A incorporates the same drug substance as prexigebersen but has a slightly modified formulation designed to enhance nanoparticle properties. In late 2019, we filed an IND application to initiate a Phase 1/1b clinical trial of prexigebersen-A in patients with solid tumors, including ovarian, endometrial, pancreatic and breast cancer. Ovarian cancer is one of the most common types of gynecologic malignancies, with approximately 50% of all cases occurring in women older than 63 years. On October 27, 2021, we announced that the FDA cleared the IND application for prexigebersen-A for the initial Phase 1/1b clinical trial, which allows us to proceed with next steps to open the clinical trial.

Our second drug candidate, BP1002, targets the protein Bcl-2, which is responsible for driving cell survival in up to 60% of all cancers. On November 21, 2019, we announced that the FDA cleared an IND application for BP1002 for an initial Phase 1 clinical trial that will evaluate the ability of BP1002 to treat refractory/relapsed lymphoma and CLL patients. The Phase 1 clinical trial is being conducted at several leading cancer centers, including MD Anderson Cancer Center and the Georgia Cancer Center. On November 19, 2020, we announced the enrollment and dosing of the first patient in the Phase 1 clinical trial.

Additionally, on August 24, 2021, we announced that the FDA cleared an IND application for BP1002 for an initial Phase 1/1b clinical trial that will evaluate the ability of BP1002 to treat refractory/relapsed AML patients. The Phase 1/1b clinical trial is anticipated to be conducted at several leading cancer centers in the United States, including the Weill Medical College, MD Anderson Cancer Center and the Georgia Cancer Center. Gail J. Roboz, M.D., will serve as Principal Investigator for the Phase 1/1b trial.

Our third drug candidate, BP1003, targets the STAT3 protein and is currently in IND enabling studies as a potential treatment of pancreatic cancer, NSCLC and AML. Preclinical models have shown BP1003 to inhibit cell viability and STAT3 protein expression in NSCLC and AML cell lines. Further, BP1003 successfully penetrated pancreatic tumors and significantly enhanced the efficacy of gemcitabine, a treatment for patients with advanced pancreatic cancer, in a pancreatic cancer patient derived tumor model. Our lead indication for BP1003 is pancreatic cancer due to the severity of this disease and the lack of effective, life-extending treatments. For example, pancreatic adenocarcinoma is projected to be the second most lethal cancer behind lung cancer by 2030. Typical survival for a metastatic pancreatic cancer patient is about three to six months from diagnosis. We successfully completed several IND enabling studies of BP1003 in 2021 and expect to complete one additional IND enabling study in 2022. If that additional study is successfully completed, our goal is to file an IND in 2022. Based on the filing of the IND, we expect to initiate the first-in-humans Phase 1 study of BP1003 in patients with refractory, metastatic solid tumors, including pancreatic cancer and NSCLC.

Our DNAbilize® technology-based products are available for out-licensing or partnering. We intend to apply our drug delivery technology template to new disease-causing protein targets to develop new nanoparticle antisense RNAi drug candidates. We have a new product identification template in place to define a process of scientific, preclinical, commercial and intellectual property evaluation of potential new drug candidates for inclusion into our drug product development pipeline. As we expand, we will look at indications where a systemic delivery is needed and antisense RNAi nanoparticles can be used to slow, reverse or cure a disease, either alone or in combination with another drug.

We have certain intellectual property as the basis for our current drug products in clinical development, prexigebersen, prexigebersen-A, BP1002 and BP1003. We are developing RNAi antisense nanoparticle drug candidates based on our own patented technology to treat cancer and autoimmune disorders where targeting a single protein may be advantageous and result in reduced patient adverse effects as compared to small molecule inhibitors with off-target and non-specific effects. We have composition of matter and method of use intellectual property for the design and manufacture of antisense RNAi nanoparticle drug products.

As of December 31, 2021, we had an accumulated deficit of $77.7 million. Our net loss was $10.4 million and $10.9 million for the years ended December 31, 2021 and 2020, respectively. We expect to continue to incur significant operating losses, and we anticipate that our losses may increase substantially as we expand our drug development programs and commercialization efforts. To achieve profitability, we must enter into license or development agreements with third parties, or successfully develop and obtain regulatory approval for one or more of our drug candidates and effectively commercialize any drug candidates we develop. In addition, if we obtain regulatory approval of one or more of our drug candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Even if we succeed in developing and commercializing one or more of our drug candidates, we may not be able to generate sufficient revenue and we may never be able to achieve or sustain profitability. We expect to finance our foreseeable cash requirements through cash on hand, cash from operations, debt financings and public or private equity offerings. We may seek to access the public or private equity markets whenever conditions are favorable; however, there can be no assurance that we will be able to raise additional capital when needed or on terms that are favorable to us, if at all. Additionally, we may seek collaborations and license arrangements for our drug candidates. We currently have no lines of credit or other arranged access to debt financing.

Financial Operations Overview

Revenue

We have not generated significant revenues to date. Our ability to generate revenues from our drug candidates, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our drug candidates.

In the future, we may generate revenue from a combination of product sales, third-party grants, service agreements, strategic alliances and licensing arrangements. We expect that any revenue we generate will fluctuate due to the timing and amount of services performed, milestones achieved, license fees earned and payments received upon the eventual sales of our drug candidates, in the event any are successfully commercialized. If we fail to complete the development of any of our drug candidates or obtain regulatory approval for them, our ability to generate future revenue will be adversely affected.

Research and development expenses

Research and development expenses consist of costs associated with our research activities, including the development of our drug candidates. Our research and development expenses consist of:

- expenses related to research and development personnel, including salaries and benefits, travel and stock-based compensation;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, clinical investigative sites, laboratories, manufacturing organizations and consultants; and
- costs of materials used during research and development activities.

Costs and expenses that can be clearly identified as research and development are charged to expense as incurred. Advance payments, including nonrefundable amounts, for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts will be recognized as an expense as the related goods are delivered or the related services are performed. If the goods will not be delivered, or services will not be rendered, then the capitalized advance payment is charged to expense.

We expect research and development expenses associated with the completion of the associated clinical trials to be substantial and to increase over time. The successful development of our drug candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete development of our drug candidates or the period, if any, in which material net cash inflows from our drug candidates may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the rate of progress, results and costs of completion of ongoing clinical trials of our drug candidates;
- the size, scope, rate of progress, results and costs of completion of any potential future clinical trials and preclinical tests of our drug candidates that we may initiate;
- competing technological and market developments;
- the performance of third-party manufacturers and suppliers;
- the ability of our drug candidates, if they receive regulatory approval, to achieve market success;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our drug candidates; and

- the impact, risks and uncertainties related to COVID-19 and actions taken by governmental authorities or others in connection therewith.

A change in the outcome of any of these variables with respect to the development of a drug candidate could mean a significant change in the costs and timing associated with the development of that drug candidate. For example, if the FDA or other regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of a drug candidate or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and administrative expenses

Our general and administrative expenses consist primarily of salaries and benefits for management and administrative personnel, professional fees for legal, accounting and other services, travel costs and facility-related costs such as rent, utilities and other general office expenses.

Results of Operations

Comparisons of the Year Ended December 31, 2021 to the Year Ended December 31, 2020

Revenue. We had no revenue for each of the years ended December 31, 2021 and 2020.

Research and Development Expenses. Our research and development expense was $5.9 million for the year ended December 31, 2021, a decrease of $0.7 million compared to the year ended December 31, 2020. The decrease in research and development expense was primarily due to timing of activities related to our clinical trial for prexigebersen in AML partially offset by an increase in manufacturing expenses related to drug product batch releases in the fourth quarter of 2021. The following table sets forth our research and development expenses (in thousands):

	Year ended December 31,	
	2021	2020
Research and development expense	$ 5,744	$ 6,477
Non-cash stock-based compensation expense	166	101
Total research and development expense	$ 5,910	$ 6,578

General and Administrative Expenses. Our general and administrative expense was $4.5 million for the year ended December 31, 2021, an increase of $0.2 million compared to the year ended December 31, 2020. The increase in general and administrative expense was primarily due to increased stock-based compensation expense. The following table sets forth our general and administrative expenses (in thousands):

	Year ended December 31,	
	2021	2020
General and administrative expense	$ 3,878	$ 3,854
Non-cash stock-based compensation expense	655	476
Total general and administrative expense	$ 4,533	$ 4,330

Net Operating Loss. Our net loss from operations was $10.4 million for the year ended December 31, 2021, a decrease of $0.4 million compared to the year ended December 31, 2020.

Net Loss. Our net loss was $10.4 million for the year ended December 31, 2021, a decrease of $0.4 million compared to the year ended December 31, 2020.

Net Loss per Share. Net loss per share, both basic and diluted, was $1.55 per share for the year ended December 31, 2021, compared to $2.83 per share for the year ended December 31, 2020. Net loss per share is calculated using the weighted average

number of shares of common stock outstanding during the applicable periods and excludes stock options and warrants because they are antidilutive.

Liquidity and Capital Resources

Overview

We have not generated significant revenues to date. Since our inception, we have funded our operations primarily through public and private offerings of our capital stock and other securities. We expect to finance our foreseeable cash requirements through cash on hand, cash from operations, debt financings and public or private equity offerings. We may seek to access the public or private equity markets whenever conditions are favorable; however, there can be no assurance that we will be able to raise additional capital when needed or on terms that are favorable to us, if at all. Additionally, we may seek collaborations and license arrangements for our drug candidates. We currently have no lines of credit or other arranged access to debt financing.

We had a cash balance of $23.8 million at December 31, 2021, an increase of $10.0 million compared to December 31, 2020. We believe that our available cash at December 31, 2021 will be sufficient to meet obligations and fund our liquidity and capital expenditure requirements for at least the next 12 months from the date of this Annual Report on Form 10-K.

Cash Flows

For the Year Ended December 31, 2021

Operating Activities. Net cash used in operating activities for the year ended December 31, 2021 was $9.9 million. Excluding non-cash stock-based compensation expense of $0.8 million and depreciation and amortization expenses of $0.2 million, net cash used in operating activities consisted primarily of the net loss for the period of $10.4 million, an increase in current assets of $0.2 million and a decrease in operating liabilities of $0.3 million.

Investing Activities. Net cash used in investing activities for the year ended December 31, 2021 consisted of capital expenditures totaling $0.1 million which were related to research and development equipment purchases and a website upgrade.

Financing Activities. Net cash provided by financing activities for the year ended December 31, 2021 was $20.0 million. Net cash provided by financing activities consisted primarily of net proceeds of $12.2 million from the 2021 Public Offering and net proceeds of $3.7 million from sales of our common stock under the Offering Agreement, each as described below, as well as net proceeds of $4.2 million from the exercise of warrants to purchase shares of our common stock.

For the Year Ended December 31, 2020

Operating Activities. Net cash used in operating activities for the year ended December 31, 2020 was $11.0 million. Excluding non-cash stock-based compensation expense of $0.6 million and depreciation and amortization expenses of $0.2 million, net cash used in operating activities consisted primarily of the net loss for the period of $10.9 million, an increase in current assets of $0.6 million and a decrease in operating liabilities of $0.2 million.

Investing Activities. There were no investing activities for the year ended December 31, 2020.

Financing Activities. Net cash provided by financing activities for the year ended December 31, 2020 consisted primarily of net proceeds of $4.3 million from the offer and sale of shares of our common stock under the Offering Agreement, as described below.

2019 Shelf Registration Statement

On May 16, 2019, we filed a shelf registration statement on Form S-3 with the SEC, which was declared effective by the SEC on June 5, 2019 (File No. 333-231537) (the "2019 Shelf Registration Statement"), at which time the offering of unsold securities under a previous shelf registration statement on Form S-3 filed with the SEC, which was declared effective by the SEC on January 9, 2017 (File No. 333-215205), was deemed terminated pursuant to Rule 415(a)(6) under the Securities Act. The 2019 Shelf Registration Statement was filed to register the offering, issuance and sale of (i) up to $125.0 million of our common stock, preferred stock,

warrants to purchase common stock or preferred stock or any combination thereof, either individually or in units, and (ii) up to 5,149 shares of our common stock pursuant to the exercise of warrants that were issued in connection with a registered direct offering in 2016. Because our public float is less than $75 million, our ability to offer and sell any securities under the 2019 Shelf Registration Statement is currently limited pursuant to Instruction I.B.6 to Form S-3. For so long as the Company's public float is less than $75 million, the aggregate market value of securities sold by the Company under the 2019 Shelf Registration Statement pursuant to Instruction I.B.6 to Form S-3 during any 12 consecutive months may not exceed one-third of the Company's public float. The foregoing does not constitute an offer to sell or the solicitation of an offer to buy securities, and shall not constitute an offer, solicitation or sale in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of that jurisdiction.

At-The-Market Offering Agreement

On July 13, 2020, we entered into an At-The-Market Offering Agreement (the "Offering Agreement") with H. C. Wainwright & Co., LLC ("Wainwright"), as sales agent and/or principal, pursuant to which we may offer and sell, from time to time, through or to Wainwright, shares of our common stock. Sales of shares of common stock under the Offering Agreement were previously made pursuant to the 2019 Shelf Registration Statement and a related prospectus supplement filed with the SEC on July 14, 2020, for an aggregate offering price of up to $7.0 million. From and after August 18, 2021, sales of shares of common stock under the Offering Agreement will be made pursuant to the 2019 Shelf Registration Statement and a related prospectus supplement filed with the SEC on August 18, 2021, for an aggregate offering price of up to $10.0 million, provided that we may be limited in the amount of securities that we can sell under the Offering Agreement pursuant to Instruction I.B.6 to Form S-3 for so long as our public float remains less than $75.0 million. Under the Offering Agreement, Wainwright may sell shares by any method deemed to be an "at the market" offering as defined in Rule 415 under the Securities Act. We will pay Wainwright a commission of 3% of the aggregate gross proceeds from each sale of shares under the Offering Agreement and have agreed to provide Wainwright with customary indemnification and contribution rights. We have also agreed to reimburse Wainwright for certain specified expenses. During the year ended December 31, 2021, we offered and sold 478,800 shares of our common stock under the Offering Agreement for net proceeds of approximately $3.7 million. As of December 31, 2021, we had offered and sold 1,328,800 shares of our common stock under the Offering Agreement for gross proceeds of approximately $8.4 million. The net proceeds from the offering, after deducting commissions and our offering expenses, were approximately $8.0 million.

2021 Public Offering

On February 16, 2021, we entered into a placement agency agreement with Roth Capital Partners, LLC relating to a public offering of 1,710,600 shares of our common stock for gross proceeds of approximately $13.0 million under the 2019 Shelf Registration Statement (the "2021 Public Offering"). In addition, on February 16, 2021, we entered into a securities purchase agreement with certain institutional investors pursuant to which we agreed to sell an aggregate of 1,650,000 shares of our common stock in the 2021 Public Offering to such investors. The 2021 Public Offering closed on February 18, 2021. The net proceeds from the 2021 Public Offering, after deducting the placement agent's fees and expenses and our offering expenses, were approximately $12.2 million.

Future Capital Requirements

We expect to continue to incur significant operating expenses in connection with our ongoing activities, including conducting clinical trials, manufacturing and seeking regulatory approval of our drug candidates, prexigebersen, prexigebersen-A, BP1002 and BP1003. Accordingly, we will continue to require substantial additional capital to fund our projected operating requirements. Such additional capital may not be available when needed or on terms favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current and future operating plan. There can be no assurance that we will be able to continue to raise additional capital through the sale of our securities in the future. Our future capital requirements may change and will depend on numerous factors, which are discussed in detail in "Item 1A. Risk Factors" of this Annual Report on Form 10-K.

Off-Balance Sheet Arrangements

As of December 31, 2021, we did not have any material off-balance sheet arrangements.

Critical Accounting Policies

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in conformity with GAAP in the U.S. The preparation of such financial statements has required our management to make assumptions, estimates and judgments that affect the amounts reported in the financial statements, including the notes thereto, and related disclosures of commitments and contingencies, if any. We consider our critical accounting policies to be those that require the more significant judgments and estimates in the preparation of financial statements, including the following:

Research and Development Costs – Costs and expenses that can be clearly identified as research and development are charged to expense as incurred. Advance payments, including nonrefundable amounts, for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts will be recognized as an expense as the related goods are delivered or the related services are performed. If the goods will not be delivered, or services will not be rendered, then the capitalized advance payment is charged to expense.

The Company estimates its clinical trial expense accrual each period based on a cost per patient calculation which is derived from estimated start-up costs, clinical trial costs based on the number of patients and length of treatment and clinical study report costs. These services are performed by the Company's third-party clinical research organizations, laboratories and clinical investigative sites. The expense accrual is recorded in research and development expense each period. Amounts that have been prepaid in advance of work performed are recorded in other current assets.

For the year ended December 31, 2021 and 2020, we had $5.9 million and $6.6 million, respectively, of costs classified as research and development expense.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not applicable.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our consolidated financial statements, together with the report of our independent registered public accounting firm, are set forth beginning on page F-1 of this Annual Report on Form 10-K.

ITEM 9. CHANGES AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

It is management's responsibility to establish and maintain adequate disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Disclosure controls and procedures are controls and other procedures of a company that are designed to ensure that information required to be disclosed by the company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to management, including the company's principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure.

Our management, including our Chief Executive Officer (who is also our Chief Financial Officer), has reviewed and evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of the end of the period covered by this Annual Report on Form 10-K. Following this review and evaluation, our management determined that as of the end of the period covered by this Annual Report on Form 10-K, our disclosure controls and procedures were

effective to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms, and is accumulated and communicated to management, including our Chief Executive Officer and our Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting, as defined in Rule 13a-15(f) under the Exchange Act, is a process designed by, or under the supervision of, our principal executive officer and our principal financial officer, and effected by our Board, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and disposition of our assets;

- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and

- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. The scope of management's assessment of the effectiveness of internal control over financial reporting includes our consolidated subsidiary.

Management's assessment of the effectiveness of our internal controls is based principally on our financial reporting as of December 31, 2021. In making our assessment of internal control over financial reporting, management used the criteria set forth in *Internal Control – Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Our management, with the participation of our Chief Executive Officer (who is also our Chief Financial Officer), has evaluated the effectiveness of our internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, as of December 31, 2021. Based on this evaluation, management believes that, as of December 31, 2021, our internal control over financial reporting was effective.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the fourth fiscal quarter of 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Identification of Directors and Executive Officers

Our current directors and officers are set forth below:

Name	Age	Position - Committee
Peter H. Nielsen	73	Chief Executive Officer; President; Chief Financial Officer; Treasurer; Chairman of the Board; Director – Business Development Committee
Heath W. Cleaver, CPA	48	Director – Audit Committee (Chair); Compensation Committee; Nominating/Corporate Governance Committee (Chair)
Paul D. Aubert	52	Director – Audit Committee; Compensation Committee -Chair; Nominating/Corporate Governance Committee
Douglas P. Morris	66	Director – Business Development Committee; Director of Investor Relations; Secretary

Our current directors will serve until the next annual meeting of stockholders or until their successors are elected or appointed and qualified.

Background Information

Peter H. Nielsen. Mr. Nielsen co-founded Bio-Path and has served as Bio-Path's President, Chief Executive Officer, Chief Financial Officer/Treasurer and Chairman of the Board since 2008. At the time of Bio-Path's establishment in 2007, Mr. Nielsen licensed technology and targets from The University of Texas, MD Anderson Cancer Center and coordinated preclinical development, optimization and manufacturing of Bio-Path's lead drug candidate, prexigebersen. Since that time, Mr. Nielsen has led the clinical advancement of prexigebersen into Phase 2 studies, the introduction of additional pipeline candidates and the Company's public market debut. Prior to co-founding Bio-Path, Mr. Nielsen worked with several other companies, leading turnarounds and developing and executing on strategies for growth. Mr. Nielsen previously served as a director of Synthecon, Inc., a company developing 3D cell culture technology. Before entering the biotechnology sector, Mr. Nielsen was a lieutenant in the U.S. Naval Nuclear Power program where he was director of the physics department and was employed at Ford Motor Company in product development. Mr. Nielsen has a broad background in senior management and has significant negotiating experience. He holds engineering, mathematics and M.B.A. finance degrees from the University of California at Berkeley.

Heath W. Cleaver, CPA. Mr. Cleaver has served as a director of Bio-Path since 2014. Since February 2020, Mr. Cleaver has served as the President and Chief Financial Officer of Compressor Engineering Corporation ("CECO"), a privately-held independent manufacturer of engine and compressor replacement parts. Prior to his current roles, Mr. Cleaver served as Chief Financial Officer of CECO from July 2017 to February 2020. Mr. Cleaver was previously a consultant providing turn-around management and capital raising services to companies in the oil and gas service sector from 2016 to 2017. From 2015 to 2016, Mr. Cleaver served as the Chief Financial Officer of Global Fabrication Services, Inc. In 2014, Mr. Cleaver served as Chief Financial Officer at Tarka Resources, Inc. From 2011 until 2014, Mr. Cleaver served as Chief Financial Officer of Porto Energy Corp. From 2010 until 2011, Mr. Cleaver served as Chief Accounting Officer of Porto Energy Corp. Mr. Cleaver served as Corporate Controller and then as Vice President and Chief Accounting Officer for BPZ Energy from 2006 to 2010. Beginning in 1997 through 2004, Mr. Cleaver served in various accounting roles, including Financial Controller, at Horizon Offshore Contractors, Inc. Mr. Cleaver is a Certified Public Accountant in the state of Texas and holds a Bachelor's Degree in Business Administration - Accounting from Texas A&M University.

Paul D. Aubert. Mr. Aubert was appointed to the Board on February 1, 2018. Mr. Aubert is currently Senior Vice President & General Counsel of Anthem Holdings Company and its subsidiaries, positions he has held since March 2018. From June 2014 to March 2018, he practiced law in a solo law practice and also served as part-time General Counsel to his current employers. From February 2012 through May 2014, Mr. Aubert served as General Counsel of Pernix Therapeutics Holdings, Inc., a Nasdaq-listed specialty pharmaceutical company. Before that, he was a Shareholder in the Corporate and Securities practice group at Winstead PC, a national law firm headquartered in Dallas, Texas, from 2007 to 2012. Mr. Aubert also served as an attorney in the Corporate and Securities practice groups of several national and international law firms prior to joining Winstead in 2004, including at Andrews Kurth LLP from 1999 to 2004, Weil, Gotshal & Manges LLP from 1998 to 1999 and Jones Walker LLP from 1996 to 1998. Mr. Aubert holds a Juris Doctor and an M.B.A. from Tulane University in New Orleans, Louisiana and a B.A. in History from Louisiana State University - Baton Rouge.

Douglas P. Morris. Mr. Morris is a co-founder of Bio-Path and has served as a director of Bio-Path since 2007 and served as an officer from 2007 to June 2014. Mr. Morris also currently serves as the Director of Investor Relations and the Secretary of Bio-Path. Mr. Morris previously served as a co-founder, Managing Member, and Secretary of nCAP Holdings, LLC (nCAP), a privately held technology based company from September 2013 to January 2016. Between 1993 and 2010, Mr. Morris was an officer and director of Celtic Investment, Inc., a financial services company. Mr. Morris owned and operated Hyacinth Resources, LLC ("Hyacinth"), a business-consulting firm, from 1990 until September 2018, and is also a Managing Member of Sycamore Ventures, LLC, a privately held consulting firm. Mr. Morris has a B.A. from Brigham Young University, and attended the University of Southern California Master's program in public administration.

Board of Directors

Our operations are managed under the broad supervision of the Board, which has ultimate responsibility for the establishment and implementation of our general operating philosophy, objectives, goals and policies. Our Board is currently comprised of two independent directors and two non-independent directors. The Board has determined that current directors Heath W. Cleaver and Paul D. Aubert are "independent" as independence is defined under the listing standards for The Nasdaq Stock Market. The Board based these determinations primarily on a review of the responses our directors provided to questions regarding employment and compensation history, affiliations and family and other relationships.

As previously reported, due solely to the Director Resignation as described in the Company's Current Report on Form 8-K filed on February 18, 2022, the Company is not in compliance with the continued listing requirements as set forth in Nasdaq Listing Rules 5605(b)(1) and 5605(c)(2)(A) regarding the composition of the Board and the Audit Committee, respectively, because a majority of the Board is not comprised of Independent Directors and the Audit Committee is not comprised of three Independent Directors. Also as previously reported, the Listing Qualifications Department of Nasdaq has granted the Company a cure period to regain compliance with such Nasdaq Listing Rules, which cure period will expire upon the earlier of the Company's next annual stockholders' meeting or February 14, 2023; provided, however, that if the Company's next annual stockholders' meeting occurs no later than 180 days following the Director Resignation, then the cure period will expire 180 days following the Director Resignation. The Board intends to appoint a new Independent Director to fill the vacancy prior to the expiration of such cure period in order to regain compliance with such Nasdaq Listing Rules.

Codes of Ethics

We have adopted the Employee Code of Business Conduct and Ethics, which applies to all of our employees, including our executive officers, and the Code of Business Conduct and Ethics for Members of the Board, which applies to members of the Board.

Board Committees

The Board has a standing audit committee (the "Audit Committee"), compensation committee (the "Compensation Committee") and nominating/corporate governance committee (the "Nominating/Corporate Governance Committee"), each of which is governed by a charter. The Board may also establish other committees from time to time as necessary to facilitate the management of the business and affairs of the Company. In 2020, the Board formed a business development committee (the "Business Development Committee") that assists the Board by advising management on its plans for business development, licensing opportunities and business partnership opportunities. In addition to these committees, we also have a Scientific Advisory Board that

serves an advisory role to management and the Board. The information below summarizes the functions of each of the committees and the Scientific Advisory Board.

Audit Committee

The Audit Committee has been structured to comply with the requirements of Section 3(a)(58)(A) of the Exchange Act. The Board has determined that the Audit Committee members have the appropriate level of financial understanding and industry specific knowledge to be able to perform the duties of the position and are financially literate and have the requisite financial sophistication as required by the applicable listing standards of The Nasdaq Stock Market.

The Audit Committee, as permitted by, and in accordance with, its charter, is responsible to periodically assess the adequacy of procedures for the public disclosure of financial information and review on behalf of the Board, and report to the Board, the results of its review and its recommendation regarding all material matters of a financial reporting and audit nature, including, but not limited to, the following main subject areas:

- financial statements, including management's discussion and analysis thereof;
- financial information in any annual information form, proxy statement, prospectus or other offering document, material change report, or business acquisition report;
- press releases regarding annual and interim financial results or containing earnings guidance;
- internal controls;
- audits and reviews our financial statements; and
- filings with securities regulators containing financial information, including our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q.

The Audit Committee appoints and sets the compensation for the independent registered public accounting firm annually and reviews and evaluates such external auditor. This external auditor reports directly to the Audit Committee. The Audit Committee establishes our hiring policies regarding current and former partners and employees of the external auditor. In addition, the Audit Committee pre-approves all audit and non-audit services undertaken by the external auditor.

The Audit Committee has direct responsibility for overseeing the work of the external auditor engaged for the purpose of preparing or issuing an auditor's report or performing other audit, review or attest services, including the resolution of disagreements between the external auditor and management.

The Audit Committee is comprised of Messrs. Cleaver and Aubert. Mr. Cleaver currently serves as the chair of the Audit Committee. The Board has determined that Mr. Cleaver qualifies as an "audit committee financial expert" under the Exchange Act and that each member of the Audit Committee is an independent director. The Audit Committee meets at least once per fiscal quarter to fulfill its responsibilities under its charter and in connection with the review of the Company's quarterly and annual financial statements.

Compensation Committee

The Compensation Committee's role is to assist the Board in fulfilling its responsibilities relating to all forms of compensation of the Company's executive officers, administering the Company's incentive compensation plan and other benefits plans, including a deferred compensation plan, if applicable, and producing any required report on executive compensation for use in the Company's proxy statement or other public disclosure. The Compensation Committee operates under a written charter adopted by the Board. The Compensation Committee periodically assesses compensation of our executive officers in relation to companies of comparable size, industry and complexity, taking the performance of the Company and such other companies into consideration. All decisions with respect to the compensation of our Chief Executive Officer are determined and approved either solely by the

Compensation Committee or together with other independent directors, as directed by the Board. All decisions with respect to non-CEO executive compensation, and incentive-compensation and equity-based plans are first approved by the Compensation Committee and then submitted, together with the Compensation Committee's recommendation, to the members of the Board for final approval. In addition, the Compensation Committee will, as appropriate, review and approve public or regulatory disclosure respecting compensation, including required disclosures regarding executive compensation under Item 402 of Regulation S-K, and the basis on which performance is measured. The Compensation Committee has the authority to retain and compensate any outside adviser as it determines necessary to permit it to carry out its duties. The Compensation Committee has not to date engaged the services of any executive compensation consultant. The Compensation Committee may not form or delegate authority to subcommittees without the prior approval of the Board.

The Compensation Committee is comprised of Messrs. Aubert and Cleaver, each of whom are independent under the rules of The Nasdaq Stock Market. The Compensation Committee meets as necessary. Mr. Aubert is the chair of the Compensation Committee.

Nominating/Corporate Governance Committee

The Nominating/Corporate Governance Committee's charter provides that the responsibilities of such committee include:

- evaluating, identifying and recommending nominees to the Board;
- considering written recommendations from our stockholders for nominees to the Board;
- recommending directors to serve as committee members and chairs;
- reviewing and developing corporate governance guidelines, policies and procedures for the Board;
- reviewing disclosure by the Company of matters within the Nominating/Corporate Governance Committee's mandate; and
- reviewing and evaluating the Nominating/Corporate Governance Committee's charter and efficacy.

The Nominating/Corporate Governance Committee is responsible for, among other things, identifying and recommending potential candidates for nomination to the Board. The Nominating/Corporate Governance Committee receives advice from the Board and will consider written recommendations from the stockholders of the Company respecting individuals best suited to serve as directors, and, when necessary, develops its own list of appropriate candidates for directorships. For a description of the procedures to be followed by stockholders of the Company in submitting recommendations to be considered by the Nominating/Corporate Governance Committee, see the discussion set forth below under the heading titled, "Stockholder Nominations for Directors."

The Nominating/Corporate Governance Committee is comprised of Messrs. Cleaver and Aubert, each of whom are independent under the rules of The Nasdaq Stock Market. The Nominating/Corporate Governance Committee meets at least annually, and otherwise as necessary. Mr. Cleaver is the chair of the Nominating/Corporate Governance Committee.

Business Development Committee

The Business Development Committee assists the Board by advising management on its plans for business development, licensing opportunities and business partnership opportunities. The Business Development Committee also performs other duties as directed by the Board from time to time and operates under a written charter adopted by the Board. The Business Development Committee is currently comprised of Messrs. Nielsen and Morris.

Scientific Advisory Board

The Scientific Advisory Board assists management and the Board on an advisory basis with respect to the research, development, clinical, regulatory and commercial plans and activities relating to research, manufacture, use and/or sale of our drug

candidates and products. The Scientific Advisory Board meets on an *ad hoc* basis and may attend meetings of the Board at the Board's request. The current members of the Scientific Advisory Board are Jorge Cortes, M.D, who serves as chairman, D. Craig Hooper, Ph.D., and Jason Fleming, M.D.

Availability of Committee Charters and Other Information

The charters for our Audit Committee, Compensation Committee, and Nominating/Corporate Governance Committee, as well as our Corporate Governance Guidelines, Employee Code of Business Conduct and Ethics and Code of Business Conduct and Ethics for Members of the Board, are available under the section titled "Corporate Governance" on the Investors page of the Company's website, *www.biopathholdings.com*. We intend to disclose any changes to or waivers from the Employee Code of Business Conduct and Ethics that would otherwise be required to be disclosed under Item 5.05 of Form 8-K on our website. The information on our website is not, and shall not be deemed to be, a part of this Annual Report on Form 10-K or incorporated into any other filings we make with the SEC.

We also make available on our website, free of charge, access to our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports, as well as other documents that we file with or furnish to the SEC pursuant to Sections 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after such documents are filed with, or furnished to, the SEC.

Nomination Process

It is our Board's responsibility to nominate members for election to the Board and to fill vacancies on the Board that may occur between annual meetings of stockholders. The Nominating/Corporate Governance Committee assists the Board by identifying and reviewing potential candidates for Board membership consistent with criteria approved by the Board. The Nominating/Corporate Governance Committee also annually recommends qualified candidates (which may include existing directors) for approval by the Board of a slate of nominees to be proposed for election to the Board at the annual meeting of stockholders.

In the event of a vacancy on the Board between annual meetings of our stockholders, the Board may request that the Nominating/Corporate Governance Committee identify, review and recommend qualified candidates for Board membership for Board consideration to fill such vacancies, if the Board determines that such vacancies will be filled. Our First Amended and Restated Bylaws (the "Bylaws") allow for up to fifteen directors. The Board is permitted by the Bylaws to change the number of directors by a resolution adopted by the Board.

When formulating its recommendations for potential Board nominees, the Nominating/Corporate Governance Committee seeks and considers advice and recommendations from management, other members of the Board and may seek or consider advice and recommendations from consultants, outside counsel, accountants or other advisors as the Nominating/Corporate Governance committee or the Board may deem appropriate.

Board membership criteria are determined by the Board, with input from the Nominating/Corporate Governance Committee. The Board is responsible for periodically determining the appropriate skills, perspectives, experiences and characteristics required of Board candidates, taking into account our needs and current make-up of the Board. This assessment should include appropriate knowledge, experience, and skills in areas deemed critical to understanding the Company and our business; personal characteristics, such as integrity and judgment; and the candidate's commitments to the boards of other companies. Each Board member is expected to ensure that other existing and planned future commitments do not materially interfere with the member's service as a director and that he or she devotes the time necessary to discharge his or her duties as a director.

Stockholder Nominations for Directors

The Nominating/Corporate Governance Committee will consider candidates for director nominees that are recommended by our stockholders in the same manner as Board recommended nominees, in accordance with the procedures set forth in our Bylaws. Any such nominations should be submitted to the Nominating/Corporate Governance Committee c/o Secretary, Bio-Path

Holdings, Inc., 4710 Bellaire Boulevard, Suite 210, Bellaire, Texas 77401 before the deadline set forth in the Bylaws and should be accompanied by the following information:

- appropriate biographical information, a statement as to the qualifications of the nominee and any other information relating to such nominee that is required to be disclosed pursuant to Regulation 14A under the Exchange Act (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected); and

- the Proposing Stockholder Information (as defined in the Bylaws).

Involvement in Certain Legal Proceedings

There have been no events under any bankruptcy act, no criminal proceedings and any judgments or injunctions material to the evaluation of the ability and integrity of any director or executive officer during the last ten years.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors and officers, and persons who own more than 10% of our common stock, to file initial reports of ownership and reports of changes in ownership (Forms 3, 4, and 5) of common stock with the SEC. Officers, directors and greater than 10% stockholders are required by SEC regulation to furnish us with copies of all such forms that they file.

To our knowledge, based solely on our review of the copies of such reports received by us and on written representations by certain reporting persons that no reports on Form 5 were required, we believe that during the fiscal year ended December 31, 2021, all Section 16(a) filing requirements applicable to our officers, directors and 10% stockholders were complied with in a timely manner.

ITEM 11. EXECUTIVE COMPENSATION

The Compensation Committee oversees our compensation programs for executives and all employees. The Compensation Committee understands that for the Company and its stockholders to achieve long-term success, the compensation programs need to attract, retain, develop and motivate a strong leadership team. As a result, our executive compensation programs are designed to pay for performance, enable talent attraction, retain top talent and closely align the interests of our executives with those of our stockholders. All decisions with respect to the compensation of our Chief Executive Officer are determined and approved either solely by the Compensation Committee or together with other independent directors, as directed by the Board. All decisions with respect to non-CEO executive compensation, incentive-compensation and equity-based plans are first approved by the Compensation Committee and then submitted, together with the Compensation Committee's recommendation, to the members of the Board for final approval.

This section provides important information on our executive compensation programs and explains the compensation decisions made during 2021 by the Compensation Committee for our named executive officers ("NEOs"). In the fiscal year ended December 31, 2021, our only NEO was Peter H. Nielsen, Chairman of the Board, Chief Executive Officer, Chief Financial Officer and President.

Compensation Philosophy

Our primary objective with respect to executive compensation is to design a reward system that will align executive compensation with our overall business strategies and attract and retain highly qualified executives. We intend to stay competitive in the marketplace with companies of comparable size, industry and complexity. Our compensation philosophy for executives is guided by the following principles:

- *Pay for Performance*. In making compensation decisions, we consider annual and long-term Company performance and consider the compensation of our executive officers in relation to companies of comparable size, industry and complexity, taking the performance of the Company into consideration.

- *Reviewed Annually*. The Compensation Committee annually reviews compensation levels to ensure we remain competitive and continue to attract, retain and motivate top-tier talent.

- *Alignment with Stockholder Interests*. Our compensation is intended to closely align the interests of our NEOs with those of our stockholders in an effort to create long-term stockholder value. In developing our compensation philosophy, the Compensation Committee has considered the most recent stockholder advisory vote on executive compensation in which an overwhelmingly positive percentage of the votes cast were in favor of our executive compensation. The Compensation Committee is continuously mindful of stockholders' views on executive compensation and remains focused on ensuring proper alignment with stockholder interests.

Our compensation philosophy rewards demonstrated performance and encourages behavior that is in the long-term best interests of the Company and its stockholders.

Elements and Mix of our 2021 Compensation Program

The following elements made up the fiscal year 2021 compensation program for our NEOs:

Element	Form of Compensation	Purpose, Basis and Performance Criteria
Base Salary	Cash	• Base salary is intended to provide a market competitive level of fixed compensation in recognition of responsibilities, skills, capabilities, experience and leadership. • Base salary is not generally performance based, but reflective of competencies and experience.
Annual Performance Incentive Awards (considered "at-risk" compensation)	Cash	• Annual cash performance incentive awards are intended to motivate and reward performance achievement. • Payments are discretionary and approved annually by the Compensation Committee.
Long-Term Incentive Awards (considered "at-risk" compensation)	Stock Options	• Long-term incentive awards are intended to recognize and reward the achievement of long-term corporate goals and objectives, recognize promotions, motivate retention of our leadership talent and align executives' interests with our stockholders. • The Compensation Committee determines the amount of long-term incentive awards to be granted to each NEO. The Compensation Committee also may make isolated awards to recognize promotions, new hires or individual performance achievements. • In 2021, the long-term incentive awards included time-vested equity awards that vest over a four-year period. • The Compensation Committee provides time-vested long-term incentives (i) to build a consistent ownership stake and retention incentive, (ii) to create a meaningful tie to the Company's relative long-term stockholder returns and (iii) to motivate consistent improvement over a longer-term horizon.
Change of Control Severance	Eligible to receive severance payments and post-termination health benefits in connection with involuntary termination within three months before or twelve months after a change of control	• Employment agreements are intended to provide financial security and an industry-competitive compensation package for NEOs. This additional security helps ensure that NEOs remain focused on our performance and the continued creation of stockholder value throughout any change of control transaction rather than on the potential uncertainties associated with their own employment.

Evaluation Process, Compensation Consultant, Peer Comparisons and Officers

Evaluation Process. The Compensation Committee oversees the administration of the compensation programs applicable to our employees, including our NEOs. The Compensation Committee generally makes its decisions regarding the annual compensation of our NEOs at its regularly-scheduled meeting in the first quarter of each year. These decisions include adjustments to base salary, grants of annual incentive awards and grants of long-term incentive awards. The Compensation Committee also makes compensation adjustments as necessary at other times during the year, such as in the case of promotions, changes in employment status and for competitive purposes.

Each year for the Compensation Committee meeting, our CEO prepares an evaluation of each of the other executive officers, if any, and makes compensation recommendations to the Compensation Committee based upon our performance against our corporate performance metrics and the individual's performance. In addition to considering the CEO's recommendations, the Compensation Committee assesses the applicable executive officer's impact during the year and his or her overall value to the Company, specifically by considering the individual leadership skills, impact on strategic initiatives, performance in his or her primary area of responsibility, his or her role in succession planning and development, and other intangible qualities that contribute to corporate and individual success. During 2021, our CEO was our only executive officer.

Compensation Consultant and Peer Comparisons. For the 2021 performance period, the Compensation Committee did not engage an external compensation consultant to review the compensation of our executive officers. For comparison purposes, the Compensation Committee relied upon peer executive compensation data from proxies and compensation surveys of the Industry Peer Group (as defined below) prepared by our executive compensation counsel based on parameters set by the Compensation Committee. The Compensation Committee reviewed executive compensation data from the Industry Peer Group to consider competitive pay levels and compensation practices. Such data included components such as total direct compensation, considered as the sum of base salary and annual cash performance incentive award, as well as total compensation, including long-term incentive awards.

While executive compensation data from the Industry Peer Group provides a point of reference for measurement, it is not the determinative factor for compensation decisions. The Compensation Committee does not target the compensation of our executive officers to a specific percentile of compensation provided to officers in comparable positions in our Industry Peer Group. The purpose of the comparison is not to supplant the analyses of our corporate performance and the individual performance of our executive officers that the Compensation Committee considers when making compensation decisions. Because the compensation data is just one of the several analytic tools that are used in setting executive compensation, the Compensation Committee has discretion in determining the nature and extent of its use.

The Compensation Committee established our current Industry Peer Group in 2021. With the assistance of our executive compensation counsel, the Compensation Committee reviews the composition of the peer group annually to ensure that companies are relevant for comparative purposes. In identifying companies to include in the Industry Peer Group, the Compensation Committee considered, among other things, the following:

- the industry of the companies;
- the annual revenue, market capitalization and total assets of the companies;
- the number of full-time employees of the companies;
- the market data sources that are available with respect to the companies; and
- the number of peers included in the Industry Peer Group.

For 2021, our Industry Peer Group consisted of the following companies (the "Industry Peer Group"):

- Actinium Pharmaceuticals Inc. (ATNM)
- Cellectar Biosciences, Inc. (CLRB)

- Cyclacel Pharmaceuticals Inc. (CYCC)
- Dare Bioscience, Inc. (DARE)
- Diffusion Pharmaceuticals, Inc. (DFFN)
- Neurobo Pharmaceuticals Inc. (NRBO)
- Ocuphire Pharma, Inc. (OCUP)
- PDS Biotechnology Corp. (PDSB)
- Soligenix, Inc. (SNGX)
- Sonnet Biotherapeutics Holdings, Inc. (SONN)
- Xenetic Biosciences Inc. (XBIO)

Role of the Chief Executive Officer. Annually, our CEO provides the Compensation Committee with an evaluation of his performance that is based, in large part, upon performance of the Company and as our lead representative to the investment community. The Compensation Committee evaluates our CEO on these and other criteria. The total compensation package for our CEO is based on the Compensation Committee's evaluation, and reflects his performance, the performance of the Company and competitive industry practices.

Role of Other Executive Officers. Our CEO makes recommendations to the Compensation Committee on all compensation actions (other than his own compensation) affecting our other executive officers, if any. In developing his recommendation for an executive officer, our CEO considers the self-evaluation prepared by the executive officer, the recommendations of his executive team, as well as his own evaluation. Our CEO's evaluation includes an assessment of the impact that the executive officer has had on the Company during the award year and their overall value to the Company as a senior leader. The Compensation Committee is provided with our CEO's evaluation of each executive officer's performance and contributions to the Company. The Compensation Committee considers the information and recommendations provided by our CEO and provides a recommendation to the Board for non-CEO executive officer base salary, annual cash incentive awards and grants of long-term incentive awards, which are subject to Board approval. During 2021, our CEO was our only executive officer.

2021 Performance Analysis and Compensation Decisions

In its meeting in the first quarter of each year, the Compensation Committee determines base salaries for the current year, the annual performance incentive awards for prior-year performance and the long-term incentive awards for the current year. Each element is reviewed annually, as well as at the time of a promotion, other change in responsibilities, other significant corporate events or a material change in market conditions. Variances in the amount of compensation awarded to each executive officer generally reflect differences in individual responsibility and experience.

Base Salary. In recent years, the Compensation Committee has adjusted executive base salaries with the goal of providing a stable base of competitive cash compensation while rewarding corporate and individual performance through annual performance incentive awards. During 2021, the annual base salary for Mr. Nielsen was $530,000, compared to $510,000 during 2020.

Annual Performance Incentive Awards. During 2021, the Compensation Committee approved a discretionary annual cash performance incentive award for Mr. Nielsen in the amount of $150,000.

Long-term Incentive Awards. The Compensation Committee believes that long-term incentive awards should provide for a retention incentive with a strong tie to relative long-term stockholder return. Accordingly, the Compensation Committee grants stock option awards that typically vest over a four-year period. During 2021, the Board approved a long-term incentive award in the form of stock options to Mr. Nielsen based on recommendations from the Compensation Committee. Specifically, in March 2021, Mr. Nielsen

was awarded a time-vested stock option award to purchase 100,000 shares of our common stock. The terms of the stock option grant require, among other things, that Mr. Nielsen continue to provide services over the vesting period of the options. The stock options vest over a four-year period from the date of the grant, with one-fourth (1/4) of the stock options vesting on the first anniversary of such grant, and the remaining stock options vesting thereafter in equal monthly increments equal to one-forty-eighth (1/48) of the stock options over the next three years, based on continuing service to the Company.

Summary Compensation Table

The following table sets forth information with respect to the compensation of our sole NEO for the fiscal years ended December 31, 2021 and 2020.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Option Awards ($)(1)	All Other Compensation ($)	Total ($)
Peter H. Nielsen, CEO,	2021	$ 530,000	$ 150,000	$ 622,505	$ 179 (2)	$ 1,302,684
CFO, President, Chairman, Director	2020	$ 510,000	$ 150,000	$ 427,332	$ 170 (2)	$ 1,087,502

(1) The amounts reported in this column reflect the aggregate grant date fair value of equity awards granted during the year computed in accordance with FASB ASC Topic 718. See Note 9 to our consolidated financial statements included in this Annual Report on Form 10-K for assumptions made by us in such valuation.

(2) The amounts reported represent life insurance premiums paid by the Company for Mr. Nielsen.

Grants of Plan-Based Awards Table

The following table contains information about grants of plan-based stock options to our sole NEO during fiscal year 2021:

		Estimated Future Payouts Under Non-Equity Incentive Plan Awards							
Name	Grant Date	Threshold ($)	Target ($)	Maximum ($)	All Other Stock Awards: Number of Shares of Stock or Units (#)	All Other Option Awards: Number of Securities Underlying Options (#)	Exercise or Base Price of Option Awards ($/Sh)	Grant Date Fair Value of Stock Awards ($)(2)
Mr. Nielsen (1)	3/31/2021					100,000	$ 7.02	$ 6.23

(1) Reflects time-vested stock options awarded under the 2017 Stock Incentive Plan. The options vest over a four-year period from the date of grant, with one-fourth (1/4) of the options vesting on the first anniversary of such grant, and the remaining options vesting thereafter in equal monthly increments equal to one-forty-eighth (1/48) of the options over the next three years.

(2) The amounts in this column reflect the aggregate grant date fair value of equity awards granted during the year computed in accordance with FASB ASC Topic 718. See Note 9 to our consolidated financial statements included in this Annual Report on Form 10-K for assumptions made by us in such valuation.

Narrative Disclosures to Summary Compensation Table and Grants of Plan-Based Awards Table

Please see the discussion under the heading “2021 Performance Analysis and Compensation Decisions” in this Annual Report on Form 10-K, above.

Outstanding Equity Awards at December 31, 2021

The following table sets forth certain information with respect to outstanding stock option awards of our sole NEO for the fiscal year ended December 31, 2021.

Name	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price ($)	Option Expiration Date
Mr. Nielsen (1)	7,500	—	—	$ 92.00	August 2023
Mr. Nielsen (1)	2,761	—	—	$ 550.00	April 2026
Mr. Nielsen (2)	5,961	539	—	$ 36.80	April 2028
Mr. Nielsen (3)	10,313	4,684	—	$ 18.40	March 2029
Mr. Nielsen (4)	6,562	8,438	—	$ 3.25	March 2030
Mr. Nielsen (5)	31,875	53,125	—	$ 5.21	June 2030
Mr. Nielsen (6)	—	100,000	—	$ 7.02	March 2031

(1) All of these options granted are fully vested.

(2) This option vests over a four-year period from the date of grant, April 11, 2018, with one-fourth (1/4) of the shares vesting on the first anniversary of such grant, and the remaining shares vesting thereafter in equal monthly increments equal to one-forty-eighth (1/48) of the shares over the next three years, based on continuing service to the Company.

(3) This option vests over a four-year period from the date of grant, March 28, 2019, with one-fourth (1/4) of the shares vesting on the first anniversary of such grant, and the remaining shares vesting thereafter in equal monthly increments equal to one-forty-eighth (1/48) of the shares over the next three years, based on continuing service to the Company.

(4) This option vests over a four-year period from the date of grant, March 28, 2020, with one-fourth (1/4) of the shares vesting on the first anniversary of such grant, and the remaining shares vesting thereafter in equal monthly increments equal to one-forty-eighth (1/48) of the shares over the next three years, based on continuing service to the Company.

(5) This option vests over a four-year period from the date of grant, June 16, 2020, with one-fourth (1/4) of the shares vesting on the first anniversary of such grant, and the remaining shares vesting thereafter in equal monthly increments equal to one-forty-eighth (1/48) of the shares over the next three years, based on continuing service to the Company.

(6) This option vests over a four-year period from the date of grant, March 31, 2021, with one-fourth (1/4) of the shares vesting on the first anniversary of such grant, and the remaining shares vesting thereafter in equal monthly increments equal to one-forty-eighth (1/48) of the shares over the next three years, based on continuing service to the Company.

Employment Agreement and Potential Payments Upon Termination or Change of Control

Bio-Path Subsidiary has entered into an employment agreement with its Chief Executive Officer, Peter H. Nielsen, dated May 1, 2007 (the "Nielsen Employment Agreement").

The Nielsen Employment Agreement provides for a base salary, as approved by the Compensation Committee, of $530,000. The Nielsen Employment Agreement provides that Mr. Nielsen is entitled to certain severance payments and benefits in the event he is terminated without Cause (as defined in the Nielsen Employment Agreement) or resigns for Good Reason (as defined in the Nielsen Employment Agreement), subject to Mr. Nielsen's continued compliance with the Confidentiality Agreement (as defined in the Nielsen Employment Agreement) and execution of a general release of all claims against us. In addition, the Nielsen Employment

Agreement also provides that Mr. Nielsen is entitled to certain severance payments and benefits in the event he is terminated without Cause or resigns for Good Reason within three months before or 12 months following a Change in Control (as defined in the Nielsen Employment Agreement), subject to Mr. Nielsen's continued compliance with the Confidentiality Agreement and execution of a general release of all claims against us.

The severance payments and benefits include the following in the event Mr. Nielsen is terminated without Cause or resigns for Good Reason: (i) any accrued but untaken vacation days of Mr. Nielsen will be paid to the extent not yet paid; (ii) the equivalent of Mr. Nielsen's base salary will be paid for a period of three months; and (iii) subject to certain restrictions, for three months after Mr. Nielsen's date of termination, the Company will continue its contributions toward Mr. Nielsen's health care, dental, disability and life insurance benefits on the same basis as immediately prior to the date of termination.

The severance payments and benefits include the following in the event Mr. Nielsen is terminated without Cause or resigns for Good Reason within three months before or 12 months following a Change in Control: (i) any unvested stock or stock options awarded to Mr. Nielsen shall immediately vest upon the occurrence of Mr. Nielsen's termination of employment; (ii) Mr. Nielsen's base salary will be paid through the termination date, and any accrued but untaken vacation days of Mr. Nielsen will be paid to the extent not yet paid; (iii) Mr. Nielsen's normal post-termination benefits will be paid in accordance with our retirement, insurance and other benefit plan arrangements (including non-qualified deferred compensation plans); (iv) the equivalent of Mr. Nielsen's base salary will be paid for a period of three months; (v) subject to certain restrictions, for six months after Mr. Nielsen's date of termination, or such longer period as may be provided by the terms of the appropriate plan, program, practice of policy, Mr. Nielsen's health care, dental, disability and life insurance benefits will be provided on the same basis as immediately prior to the date of termination; and (vi) subject to certain restrictions and to the extent not otherwise paid or provided, we will pay or provide any other amounts or benefits required to be paid or provided or which Mr. Nielsen is eligible to receive following his termination of employment under any of our plans, programs, policies, practices, contracts or agreements.

Potential severance payments and benefits to be paid pursuant to the Nielsen Employment Agreement assuming a termination or Change in Control occurred on December 31, 2021 are set forth in the table below.

		Triggering Event	
Name	Benefit	Termination without Cause or Resignation for Good Reason ($)	Termination without Cause or Resignation for Good Reason within 3 Months Before or 12 Months Following a Change in Control ($)
Peter H. Nielsen	Market Value of Stock Vesting	$ 7,800	$ 7,800 (1)
	Accrued Vacation Days	48,923	48,923
	Three Months' Base Salary	132,500	132,500
	Continuation of Benefits	10,589	21,178
	Total	$ 199,812	$ 210,401

(1) Mr. Nielsen's stock option awards would immediately become vested, and the value of the acceleration would be equal to the vesting shares multiplied by the excess of the then current stock price over the exercise price of the options. For purposes of this table, we have calculated the value of the acceleration using the closing price of our common stock on December 31, 2021, or $3.77 per share.

DIRECTOR COMPENSATION

The following table presents summary information for the year ended December 31, 2021 regarding the compensation of the members of our Board (other than Mr. Nielsen).

Name	Fees Earned or Paid in Cash	Option Awards	All Other Compensation	Total
Heath W. Cleaver	$ 54,750 (1)	$ 61,633 (2)	$ —	$ 116,383
Paul D. Aubert	$ 46,125 (1)	$ 61,633 (2)	$ —	$ 107,758
Martina Molsbergen (3)	$ 48,375 (1)	$ 61,633 (2)	$ 4,500 (4)	$ 114,508
Douglas P. Morris (5)	$ —	$ 81,027 (6)	$ 68,473 (7)	$ 149,500

(1) These amounts reflect cash fees paid to or earned by our non-employee directors for attending Board or committee meetings during the year ended December 31, 2021.

(2) In March 2021, our non-employee directors who were eligible at such time earned or received an annual grant of an option to purchase 10,000 shares of our common stock, which was the only grant received by such directors during 2021. The amounts in this column reflect the aggregate grant date fair value of equity awards granted during the year computed in accordance with FASB ASC Topic 718. See Note 9 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for assumptions made by us in such valuation.

(3) Ms. Molsbergen resigned from the Board on February 14, 2022.

(4) The amounts reported represent amounts earned for Board services performed beyond the normal scope of their Board or committee responsibilities.

(5) Mr. Morris was hired by the Company in 2016 as the Company's Director of Investor Relations. Accordingly, Mr. Morris is not considered a non-employee director and does not receive compensation for his services as a member of the Board.

(6) Option awards granted to Mr. Morris reflect compensation received by Mr. Morris in his capacity as the Company's Director of Investor Relations.

(7) This amount reflects compensation received by Mr. Morris in his capacity as the Company's Director of Investor Relations, which includes base salary and certain other benefits.

The following table reflects the aggregate number of outstanding options (including unexercisable options) held by our directors (other than Mr. Nielsen) as of December 31, 2021:

Director	Number of shares underlying outstanding options
Heath W. Cleaver	22,500
Paul D. Aubert	22,000
Douglas P. Morris (1)	31,640

(1) Mr. Morris's outstanding options include 3,265 options earned while serving as an executive officer of the Company. Mr. Morris ceased serving in his officer capacities in June 2014. However, Mr. Morris was hired by the Company in 2016 as the Company's Director of Investor Relations. Accordingly, Mr. Morris is not considered a non-employee director.

Narrative to Director Compensation Table

In 2021, our non-employee directors received cash and equity compensation in accordance with our non-employee director compensation structure. Directors who were also employed by the Company did not receive compensation for services as directors. We amended our compensation structure for all non-employee directors on January 1, 2021. During 2021, our compensation structure for all non-employee directors was as follows:

Cash Compensation Program

Non-employee directors received as compensation an annual cash retainer in the amount of $40,000.

The chairs of the respective Board committees also received as compensation the following amounts: (i) an annual cash retainer in the amount of $20,000 to the chair of the Audit Committee; (ii) an annual cash retainer in the amount of $10,000 to the chair of the Compensation Committee; (iii) an annual cash retainer in the amount of $8,000 to the chair of the Nominating/Corporate Governance Committee; and (iv) an annual cash retainer in the amount of $8,000 to the chair of the Business Development Committee.

Non-chair members of the respective Board committees also received as compensation the following amounts: (i) an annual cash retainer in the amount of $7,500 to each member of the Audit Committee; (ii) an annual cash retainer in the amount of $5,000 to each member of the Compensation Committee; and (iii) an annual cash retainer in the amount of $4,000 to each member of the Nominating/Corporate Governance Committee.

In addition to the foregoing cash compensation for Board and committee members, non-employee directors of the Board who spent significant time performing Board or committee service beyond the normal scope of their Board or committee responsibilities could receive up to $2,500 per diem at the discretion of the Chief Executive Officer of the Company.

Equity Compensation Program

Each non-employee director of the Board also received as compensation an annual stock option grant (a "Grant") of 10,000 shares of our common stock (the "Option Shares"). The exercise price of the Option Shares was determined by the Board, and the Option Shares vest over a one-year period from the date of the Grant, with the Option Shares vesting in equal monthly increments equal to one-twelfth (1/12) of the Option Shares, based on continuing service to the Company.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The following table sets forth information regarding shares of our common stock beneficially owned at March 3, 2022 by: (i) our sole NEO and each director; (ii) all executive officers and directors as a group; and (iii) each person known by us to beneficially own 5% or more of the outstanding shares of our common stock. The information in this table is based solely on statements in filings with the SEC or other reliable information.

Name of Beneficial Owner	Amount and Nature of Beneficial Ownership	Percent of Class
Peter H. Nielsen (1) (2)	128,002	1.79 %
Douglas P. Morris (1) (3)	23,686	*
Heath W. Cleaver (1) (4)	22,500	*
Paul D. Aubert (1) (5)	22,000	*
All officers and directors as a group (6)	196,188	2.74 %

*Less than 1%

(1) These are our NEOs and directors.

(2) Includes 25,823 shares owned of record and 102,179 shares issuable upon the exercise of options that are exercisable within 60 days.

(3) Includes 8,050 shares held by Hyacinth Resources, LLC and 121 shares held by Sycamore Ventures, LLC. Mr. Morris disclaims beneficial ownership of the shares held by Sycamore Ventures, LLC except to the extent of his pecuniary interest therein. Also includes 15,515 shares issuable upon the exercise of options that are exercisable within 60 days.

(4) All 22,500 shares are issuable upon the exercise of options that are exercisable within 60 days.

(5) All 22,000 shares are issuable upon the exercise of options that are exercisable within 60 days.

(6) Includes 33,994 shares owned of record and 182,194 shares issuable upon the exercise of options currently exercisable or will be exercisable within 60 days.

Equity Compensation Plan Information

There are no equity compensation plans that have not been approved by our stockholders. The following table contains information about our equity compensation plans in effect as of December 31, 2021 (in thousands, except per share amount).

Plan Category	Number of shares of common stock to be issued upon exercise of outstanding options, warrants and rights (1)	Weighted-average exercise price of outstanding options, warrants and rights	Number of shares of common stock remaining available for future issuance under equity compensation plans (2)
Equity compensation plans approved by stockholders	486	$ 14.58	190
Equity compensation plans not approved by stockholders	—		—

(1) 16 of the shares shown in this column are securities to be issued upon exercise of outstanding options, warrants and rights were subject to outstanding stock option awards as of December 31, 2021 that were granted under the First Amended Bio-Path Holdings, Inc. 2007 Stock Incentive Plan, as amended (the "2007 Stock Incentive Plan"). 470 of the shares shown in this column are securities to be issued upon exercise of outstanding options, warrants and rights were subject to outstanding stock option awards as of December 31, 2021 that were granted under the Bio-Path Holdings, Inc. 2017 Stock Incentive Plan, as amended (the "2017 Stock Incentive Plan").

(2) The shares shown in this column as remaining available for future issuance as of December 31, 2021 are all under the 2017 Stock Incentive Plan. The 2007 Stock Incentive Plan expired in January 2018.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Related Party Transactions

It is our policy that we will not enter into any transactions required to be disclosed under Item 404 of Regulation S-K promulgated by the SEC unless the Audit Committee first reviews and approves the transactions. The Audit Committee is required to review on an ongoing basis, and pre-approve all related party transactions before they are entered into, including those transactions that are required to be disclosed under Item 404 of Regulation S-K. Related party transactions involving a director must also be approved by the disinterested members of the Audit Committee. It is the responsibility of our employees and directors to disclose any significant financial interest in a transaction between the Company and a third party, including an indirect interest. All related party transactions shall be disclosed in our filings with the SEC as required under SEC rules.

In addition, pursuant to our codes of ethics, all employees, officers and directors of ours and our subsidiaries are prohibited from engaging in any relationship or financial interest that is an actual or potential conflict of interest with us without approval.

Employees and officers are required to provide written disclosure to their supervisors as soon as they have any knowledge of a transaction or proposed transaction with an outside individual, business or other organization that would create a conflict of interest or the appearance of one. Directors are required to disclose such information to the Board or as otherwise required by law.

For our last two fiscal years, there has not been nor is there currently proposed any transaction or series of similar transactions to which we were or are to be a party in which the amount involved exceeds the lesser of $120,000 or 1% of the average of our total assets at the end of our last two fiscal years, and in which any of our directors, executive officers, persons who we know hold more than 5% of our common stock, or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest other than: (i) compensation agreements and other arrangements, which are described elsewhere in this Annual Report on Form 10-K and (ii) the transactions described in the following paragraph.

We have entered into indemnity agreements with certain of our officers and directors which provide, among other things, that we will indemnify such officer or director, under the circumstances and to the extent provided for therein, for expenses, damages, judgments, fines and settlements he or she may be required to pay in actions or proceedings which he or she is or may be made a party by reason of his or her position as a director, officer or other agent of the Company, and otherwise to the fullest extent permitted under applicable law, our Certificate of Incorporation and our Bylaws.

Director Independence

The following members of the Board have been identified as independent under the standards of The Nasdaq Stock Market: Heath W. Cleaver and Paul D. Aubert. Martina Molsbergen was identified as independent under the standards of The Nasdaq Stock Market prior to the Director Resignation. Presently, there are no directors on our Audit Committee, Nominating/Corporate Governance Committee or Compensation Committee who are not independent under the standards of The Nasdaq Stock Market.

As previously reported, due solely to the Director Resignation as described in the Company's Current Report on Form 8-K filed on February 18, 2022, the Company is not in compliance with the continued listing requirements as set forth in Nasdaq Listing Rules 5605(b)(1) and 5605(c)(2)(A) regarding the composition of the Board and the Audit Committee, respectively, because a majority of the Board is not comprised of Independent Directors and the Audit Committee is not comprised of three Independent Directors. Also as previously reported, the Listing Qualifications Department of Nasdaq has granted the Company a cure period to regain compliance with such Nasdaq Listing Rules, which cure period will expire upon the earlier of the Company's next annual stockholders' meeting or February 14, 2023; provided, however, that if the Company's next annual stockholders' meeting occurs no later than 180 days following the Director Resignation, then the cure period will expire 180 days following the Director Resignation. The Board intends to appoint a new Independent Director to fill the vacancy prior to the expiration of such cure period in order to regain compliance with such Nasdaq Listing Rules.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

On March 5, 2020, the Company, at the direction of the Audit Committee, chose not to renew the engagement of BDO USA, LLP ("BDO"), which was then serving as the Company's independent registered public accounting firm. The Company notified BDO on March 6, 2020 that it would be dismissed as the Company's independent registered public accounting firm, effective immediately. The decision to change independent registered public accounting firms was approved by the Audit Committee. On March 9, 2020, the Audit Committee approved the appointment of Ernst & Young LLP ("EY") as the Company's new independent registered public accounting firm.

For the interim period from January 1, 2020 through March 6, 2020, BDO, as our independent registered public accounting firm during such time, billed the approximate fees set forth in the first table below. During the interim period from March 9, 2020 through December 31, 2020, and for the fiscal year ended December 31, 2021, EY, as our independent registered public accounting firm during such time, billed the approximate fees set forth in the second table below. The Board has considered the respective services provided by BDO and EY and has concluded that such services are compatible with the independence of BDO and EY as our principal accountants during the respective periods.

The table below sets forth the aggregate fees billed to the Company by BDO for services rendered in the interim period from January 1, 2020 through March 6, 2020 (in thousands).

	January 1, 2020 – March 6, 2020
Audit fees (1)	$ —
Audit-related fees (2)	—
Tax fees (3)	—
All other fees (4)	—
Total	$ —

(1) Audit fees consist of fees billed for professional services rendered for the audit of our consolidated financial statements, reviews of the interim condensed consolidated financial statements included in quarterly filings, services associated with equity offerings, including with respect to registration statements filed by the Company, and services that are normally provided by BDO in connection with statutory and regulatory filings or engagements, including consents, except those not required by statute or regulation.

(2) Audit-related fees consist of fees billed by BDO for assurance and related services. These fees include services provided in conjunction with due diligence services and employee benefit plan audits.

(3) Tax fees consist of fees billed for professional services rendered by BDO for state and federal tax compliance and advice, and tax planning.

(4) All other fees consist of fees billed by BDO for professional services other than those relating to audit fees, audit-related fees and tax fees.

The table below sets forth the aggregate fees billed to the Company by EY for services rendered in the interim period from March 9, 2020 through December 31, 2020 and in the fiscal year ended December 31, 2021 (in thousands).

	December 31, 2021	March 9, 2020 – December 31, 2020
Audit fees (1)	$ 285	$ 272
Audit-related fees (2)	—	—
Tax fees (3)	—	—
All other fees (4)	—	—
Total	$ 285	$ 272

(1) Audit fees consist of fees billed for professional services rendered for the audit of our consolidated financial statements, reviews of the interim condensed consolidated financial statements included in quarterly filings, services associated with equity offerings, including with respect to registration statements filed by the Company, and services that are normally provided by EY in connection with statutory and regulatory filings or engagements, including consents, except those not required by statute or regulation.

(2) Audit-related fees consist of fees billed by EY for assurance and related services. These fees include services provided in conjunction with due diligence services and employee benefit plan audits.

(3) Tax fees consist of fees billed for professional services rendered by EY for state and federal tax compliance and advice, and tax planning.

(4) All other fees consist of fees billed by EY for professional services other than those relating to audit fees, audit-related fees and tax fees.

Pre-Approval Policies and Procedures

The Audit Committee has not adopted any blanket pre-approval policies and procedures. Instead, the Audit Committee will pre-approve the provision of all audit or non-audit services.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

1. *Financial Statements*. The financial statements and information required by "Item 8. Financial Statements and Supplementary Data" of this Annual Report on Form 10-K appear on pages F-1 through F-17 of this report. The Index to Consolidated Financial Statements appears on page F-1.

2. *Financial Statement Schedules*. All schedules are omitted because they are not applicable or the required information is shown in the financial statements or the notes thereto.

3. *Exhibits.*

Exhibit Number	Exhibit
2.1	Agreement and Plan of Merger and Reorganization dated September 27, 2007, by and among the Company, Biopath Acquisition Corp., a Utah corporation and wholly owned subsidiary of the registrant, and Bio-Path, Inc., a Utah corporation (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K filed on September 27, 2007).
3.1	Certificate of Incorporation (incorporated by reference to Exhibit 3.3 to the Company's Current Report on Form 8-K filed on January 6, 2015).
3.2	Certificate of Amendment to the Certificate of Incorporation of Bio-Path Holdings, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on February 9, 2018).
3.3	Certificate of Amendment to the Certificate of Incorporation of Bio-Path Holdings, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on January 16, 2019).
3.4	First Amended and Restated Bylaws (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on June 7, 2017).
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Annual Report on Form 10-K filed on March 16, 2015).
4.2	Form of Warrant issued to Maxim Group LLC, Sabby Healthcare Volatility Master Fund, Ltd. and Sabby Volatility Warrant Master Fund, Ltd. (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K on January 21, 2014).
4.3	Form of Warrant issued to certain investors (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on June 29, 2016).
4.4	Form of Warrant issued to H.C. Wainwright & Co., LLC and certain of its designees (incorporated by reference to Exhibit 4.5 to the Company's Quarterly Report on Form 10-Q filed on August 9, 2016).
4.5	Form of New Warrant (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on May 22, 2017).
4.6	Form of Warrant Amendment (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on June 19, 2017).
4.7	Form of Warrant issued to certain investors (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on November 6, 2017).
4.8	Form of Warrant issued to Roth Capital Partners, LLC (incorporated by reference to Exhibit 4.9 to the Company's Annual Report on Form 10-K filed on April 2, 2018).
4.9	Form of Series A Warrant issued to certain investors (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed on September 21, 2018).

4.10	Form of Warrant issued to H.C. Wainwright & Co., LLC and certain of its designees (incorporated by reference to Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q filed on November 14, 2018).
4.11	Form of Underwriter Warrant issued to H.C. Wainwright & Co., LLC and certain of its designees (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on January 16, 2019).
4.12	Form of Series A Warrant issued to certain investors (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on January 22, 2019).
4.13	Form of Warrant issued to H.C. Wainwright & Co., LLC and certain of its designees (incorporated by reference to Exhibit 4.15 to the Company's Annual Report on Form 10-K filed on March 19, 2019).
4.14	Form of Warrant issued to H.C. Wainwright & Co., LLC and certain of its designees (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on March 13, 2019).
4.15	Form of Warrant issued to certain investors (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on November 22, 2019).
4.16	Form of Warrant issued to H.C. Wainwright & Co., LLC and certain of its designees (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed on November 22, 2019).
4.17	Description of Bio-Path Holdings, Inc.'s Securities Registered under Section 12 of the Securities Exchange Act of 1934 (incorporated by reference to Exhibit 4.17 to the Company's Annual Report on Form 10-K filed on March 5, 2020).
10.1+	Employment Agreement – Peter H. Nielsen (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on February 19, 2008).
10.2+	Amended 2007 Stock Incentive Plan (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-8 filed on December 10, 2008).
10.3+	First Amendment to First Amended 2007 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 14, 2013).
10.4	Form of Securities Purchase Agreement by and between the Company, Sabby Healthcare Volatility Master Fund, Ltd. and Sabby Volatility Warrant Master Fund, Ltd. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 21, 2014).
10.5	Form of Waiver, Consent and Amendment to that certain Securities Purchase Agreement by and between Sabby Healthcare Volatility Master Fund, Ltd. and Sabby Volatility Warrant Master Fund, Ltd. (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K on January 21, 2014).
10.6+	First Amendment to Employment Agreement, dated March 26, 2014 – Peter H. Nielsen (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on March 26, 2014).
10.7	Lease Agreement dated April 16, 2014 by and between the Company and Pin Oak North Parcel TT, LLC (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on April 18, 2014).
10.8	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on April 16, 2015).
10.9	Controlled Equity OfferingSM Sales Agreement, dated June 24, 2015, by and between the Company and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed on June 25, 2015).
10.10	Form of Securities Purchase Agreement by and between the Company and certain investors (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 29, 2016).
10.11	Form of Warrant Exercise Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on May 22, 2017).
10.12	Form of Securities Purchase Agreement by and between the Company and certain investors (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 6, 2017).
10.13	Form of Leak-Out Agreement by and between the Company and certain investors (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on November 6, 2017).
10.14+	Bio-Path Holdings, Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 27, 2017).
10.15	Form of Incentive Stock Option Award Agreement under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on December 27, 2017).
10.16	Form of Non-Qualified Stock Option Award Agreement under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed on December 27, 2017).
10.17	Form of Restricted Share Unit Award Agreement (Time-Vested) under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed on December 27, 2017).

10.18	Form of Restricted Share Unit Award Agreement (Performance-Based) under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed on December 27, 2017).
10.19	Form of Restricted Share Award Agreement under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Company's Current Report on Form 8-K filed on December 27, 2017).
10.20	Form of Stock Appreciation Right Award Agreement under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to the Company's Current Report on Form 8-K filed on December 27, 2017).
10.21	Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on September 21, 2018).
10.22	Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 22, 2019).
10.23	Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on March 13, 2019).
10.24	First Amendment to Lease Agreement dated April 16, 2014 by and between the Company and Pin Oak North Parcel TT, LLC (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 4, 2019).
10.25	Form of Securities Purchase Agreement by and between the Company and certain investors (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 22, 2019).
10.26	First Amendment to Bio-Path Holdings, Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 23, 2019).
10.27	Second Amendment to Bio-Path Holdings, Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 14, 2020).
10.28	At-the-Market Offering Agreement, by and between the Company and H.C. Wainwright & Co., LLC, dated July 13, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 14, 2020).
10.29	Form of Securities Purchase Agreement by and between the Company and certain investors (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on February 17, 2021).
21.1	Subsidiaries of Bio-Path Holdings, Inc. (incorporated by reference to Exhibit 21.1 to the Company's Annual Report on Form 10-K filed on March 5, 2020).
23.1*	Consent of Ernst & Young LLP.
31*	Certification of Principal Executive Officer/Principal Financial Officer pursuant to Exchange Act Rules 13a-14 and 15d-14, as adopted pursuant to Section 302 Sarbanes Oxley Act of 2002.
32**	Certification of Principal Executive Officer/Principal Financial Officer pursuant to Section 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2002.
101*	The following financial statements from the Company's Annual Report on Form 10-K for the year ended December 31, 2021, formatted in Inline XBRL: (i) Consolidated Balance Sheets; (ii) Consolidated Statements of Operations; (iii) Consolidated Statements of Cash Flows; (iv) Consolidated Statements of Shareholders' Equity; and (v) Notes to the Consolidated Financial Statements, tagged as blocks of text and including detailed tags.
104*	The cover page from the Company's Annual Report on Form 10-K for the year ended December 31, 2021, formatted in Inline XBRL (included as Exhibit 101).

* Filed herewith.

** Furnished herewith.

+ Management contract or compensatory plan.

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, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

BIO-PATH HOLDINGS, INC.

Dated: March 10, 2022

By: /s/ Peter H. Nielsen
Peter H. Nielsen
President
Chief Executive Officer
Chief Financial Officer
Principal Accounting Officer

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

Date	Title	Signature
March 10, 2022	President/Chief Executive Officer/ Chief Financial Officer/ Principal Accounting Officer/Director	/s/ Peter H. Nielsen Peter H. Nielsen
March 10, 2022	Director	/s/ Heath W. Cleaver Heath W. Cleaver
March 10, 2022	Director	/s/ Paul D. Aubert Paul D. Aubert
March 10, 2022	Director	/s/ Douglas P. Morris Douglas P. Morris

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Bio-Path Holdings, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Bio-Path Holdings, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations, shareholders' equity and cash flows for each of the two years in the period ended December 31, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosure to which it relates.

Prepaid or Accrued Research and Development Expenses

Description of the Matter	During 2021, the Company incurred $5.9 million for research and development expenses and as of December 31, 2021 recorded prepaid clinical trial expenses of $1.4 million. As disclosed in Note 2 to the consolidated financial statements, research and development costs are charged to expense when the related goods are delivered or services are performed. The Company estimated its clinical trial expense based on a cost per patient calculation, which is derived from estimated start-up costs, clinical trial costs based on the number of patients and length of treatment and clinical study report costs. The Company recorded an accrual or prepaid for clinical trial expenses based on its estimated clinical trial expense as compared to payments made to the Company's third-party clinical

research organization, laboratories and clinical investigation sites. As of December 31, 2021, all of the Company's clinical trials were in a prepaid position.

Auditing the Company's accrued and prepaid research and development expenses is complex due to significant judgment and estimates made by management in determining the clinical trial expenses incurred, which include inputs such as number of patients, length of treatment and clinical study report costs, compared to payments the Company has made.

How We Addressed the Matter in Our Audit

To test the prepaid research and development expenses for significant clinical trials, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating the significant assumptions that are used by management to estimate the recorded prepayments. To test the significant assumptions, we corroborated the patient enrollment, length of treatment, trial timeline and progress of research and development activities through discussion with the Company's research and development personnel that oversee the research and development projects, inspected the Company's contracts with third parties and any pending change orders to assess the impact on amounts recorded, and obtained information directly from vendors of their costs incurred to date. We tested a sample of transactions and compared the costs against related invoices and contracts. We also performed analytics over fluctuations in accruals or prepaid balances by trial throughout the year and tested subsequent payments to evaluate the completeness of the research and development expenses recognized.

/s/ Ernst & Young LLP

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

Houston, Texas

March 10, 2022

BIO-PATH HOLDINGS, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except par value)

	As of December 31, 2021	As of December 31, 2020
Assets		
Current assets		
Cash	$ 23,774	$ 13,755
Prepaid drug product	523	1,273
Other current assets	1,843	928
Total current assets	26,140	15,956
Fixed assets		
Furniture, fixtures & equipment	1,099	1,029
Less accumulated depreciation	(874)	(798)
	225	231
Right of use operating assets	203	288
Total Assets	$ 26,568	$ 16,475
Liabilities & Shareholders' Equity		
Current liabilities		
Accounts payable	$ 106	$ 100
Accrued expenses	770	975
Current portion of lease liabilities	82	94
Total current liabilities	958	1,169
Noncurrent lease liabilities	153	236
Total Liabilities	1,111	1,405
Shareholders' equity		
Preferred stock, $.001 par value; 10,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $.001 par value; 200,000 shares authorized; 7,160 and 4,542 shares issued and outstanding, respectively	7	5
Additional paid in capital	103,111	82,286
Accumulated deficit	(77,661)	(67,221)
Total shareholders' equity	25,457	15,070
Total Liabilities & Shareholders' Equity	$ 26,568	$ 16,475

SEE ACCOMPANYING NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

BIO-PATH HOLDINGS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except per share amounts)

	Year Ended December 31,	
	2021	**2020**
Operating expenses		
Research and development	$ 5,910	$ 6,578
General and administrative	4,533	4,330
Total operating expenses	10,443	10,908
Net operating loss	$ (10,443)	$ (10,908)
Other income		
Interest income	3	26
Total other income	3	26
Net loss	$ (10,440)	$ (10,882)
Net loss per share, basic and diluted	$ (1.55)	$ (2.83)
Basic and diluted weighted average number of common shares outstanding	6,725	3,847

SEE ACCOMPANYING NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

BIO-PATH HOLDINGS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2021	**2020**
Cash flow from operating activities		
Net loss	$ (10,440)	$ (10,882)
Adjustments to reconcile net loss to net cash used in operating activities		
Stock-based compensation	821	577
Amortization of right of use assets	85	79
Depreciation	76	72
(Increase) decrease in operating assets		
Prepaid drug product	750	(497)
Other current assets	(915)	(140)
Increase (decrease) in operating liabilities		
Accounts payable and accrued expenses	(199)	(84)
Lease liabilities	(95)	(85)
Net cash used in operating activities	(9,917)	(10,960)
Cash flow from investing activities		
Purchases of furniture, fixtures & equipment	(70)	—
Net cash used in investing activities	(70)	—
Cash flow from financing activities		
Net proceeds from sale of common stock	15,849	4,289
Net proceeds from exercise of warrants	4,157	—
Net cash provided by financing activities	20,006	4,289
Net increase (decrease) in cash	**10,019**	**(6,671)**
Cash, beginning of period	13,755	20,426
Cash, end of period	$ 23,774	$ 13,755

SEE ACCOMPANYING NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

BIO-PATH HOLDINGS, INC.

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(in thousands)

Description	Common Stock Shares	Common Stock Amount	Additional Paid in Capital	Accumulated Deficit	Total
Balance at December 31, 2019	**3,692**	$ 4	**$ 77,421**	**$ (56,339)**	**$ 21,086**
Issuance of common stock, net of fees	850	1	4,288	—	**4,289**
Stock-based compensation	—	—	577	—	577
Net loss	—	—	—	(10,882)	(10,882)
Balance at December 31, 2020	**4,542**	$ **5**	**$ 82,286**	**$ (67,221)**	**$ 15,070**
Balance at December 31, 2020	**4,542**	$ **5**	**$ 82,286**	**$ (67,221)**	**$ 15,070**
Issuance of common stock, net of fees	2,189	2	15,847	—	15,849
Exercise of warrants, net of fees	429	—	4,157	—	4,157
Stock-based compensation	—	—	821	—	821
Net loss	—	—	—	(10,440)	(10,440)
Balance at December 31, 2021	**7,160**	$ **7**	**$ 103,111**	**$ (77,661)**	**$ 25,457**

SEE ACCOMPANYING NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Bio-Path Holdings, Inc.

Notes to Consolidated Financial Statements
December 31, 2021

Unless the context requires otherwise, references in these Notes to the Consolidated Financial Statements to "we," "our," "us," "the Company" and "Bio-Path" refer to Bio-Path Holdings, Inc. and its subsidiary. Bio-Path Holdings, Inc.'s wholly-owned subsidiary, Bio-Path, Inc., is sometimes referred to herein as "Bio-Path Subsidiary."

1. Organization and Business

The Company is a clinical and preclinical stage oncology focused RNAi nanoparticle drug development company utilizing a novel technology that achieves systemic delivery for target specific protein inhibition for any gene product that is over-expressed in disease. The Company's drug delivery and antisense technology, called DNAbilize®, is a platform that uses P-ethoxy, which is a deoxyribonucleic acid (DNA) backbone modification that is intended to protect the DNA from destruction by the body's enzymes when circulating *in vivo,* incorporated inside of a lipid bilayer having neutral charge. The Company believes this combination allows for high efficiency loading of antisense DNA into non-toxic, cell-membrane-like structures for delivery of the antisense drug substance into cells. *In vivo,* the DNAbilize® delivered antisense drug substances are systemically distributed throughout the body to allow for reduction or elimination of target proteins in blood diseases and solid tumors. Through testing in numerous animal studies and treatment in over 80 patients, the Company's DNAbilize® drug candidates have demonstrated an excellent safety profile. DNAbilize® is a registered trademark of the Company. Using DNAbilize® as a platform for drug development and manufacturing, the Company currently has four antisense drug candidates in development to treat at least five different cancer disease indications.

The Company was incorporated in May 2000 as a Utah corporation. In February 2008, Bio-Path Subsidiary completed a reverse merger with the Company, which at the time was traded over the counter and had no current operations. The prior name of the Company was changed to Bio-Path Holdings, Inc. and the directors and officers of Bio-Path Subsidiary became the directors and officers of Bio-Path Holdings, Inc. Effective December 31, 2014, the Company changed its state of incorporation from Utah to Delaware through a statutory conversion pursuant to the Utah Revised Business Corporation Act and the Delaware General Corporation Law.

The Company's operations to date have been limited to organizing and staffing the Company, acquiring, developing and securing its technology and undertaking product development for a limited number of product candidates. As the Company has not begun its planned principal operations of commercializing a product candidate, the Company's activities are subject to significant risks and uncertainties, including the potential requirement to secure additional funding, the outcome of the Company's clinical trials and failing to operationalize the Company's current drug candidates before another company develops similar products.

2. Summary of Significant Accounting Policies

Principles of Consolidation — The consolidated financial statements include the accounts of Bio-Path Holdings, Inc. and its wholly owned subsidiary Bio-Path, Inc. All intercompany accounts and transactions have been eliminated in consolidation.

Cash and Cash Equivalents — The Company considers all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents.

Concentration of Credit Risk — Financial instruments that potentially subject the Company to a significant concentration of credit risk consist of cash. The Company maintains its cash balances with one major commercial bank, JPMorgan Chase Bank. The balances are insured by the Federal Deposit Insurance Corporation (the "FDIC") up to $250,000. As a result, as of December 31, 2021, approximately $23.5 million of its cash balance was not covered by the FDIC. As of December 31, 2020, the Company had approximately $13.8 million in cash on-hand, of which approximately $13.5 million was not covered by the FDIC. To date, the Company has not incurred any losses on its cash balances.

Furniture, fixtures and equipment — Furniture, fixtures and equipment are stated at cost and depreciated using the straight-line method over the estimated useful lives of the assets. Depreciation expense was $0.1 million for each of the years ended December 31, 2021 and 2020, respectively.

The estimated useful lives are as follows:

Computers and equipment – 3 years
Furniture and fixtures – 7 years
Scientific equipment –7 years
Leasehold improvements – Lesser of useful life or lease term

Major additions and improvements are capitalized, while costs for minor replacements, maintenance and repairs that do not increase the useful life of an asset are expensed as incurred.

Long-Lived Assets — The Company's long-lived assets consist of furniture, fixtures and equipment, leasehold improvements and right-of-use operating assets. Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of the asset is measured by a comparison of the asset's carrying amount to the estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated undiscounted future cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset exceeds the fair value of the asset.

Research and Development Costs — Costs and expenses that can be clearly identified as research and development are charged to expense. Advance payments, including nonrefundable amounts, for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts will be recognized as an expense as the related goods are delivered or the related services are performed. If the goods will not be delivered, or services will not be rendered, then the capitalized advance payment is charged to expense.

The Company estimates its clinical trial expense each period based on a cost per patient calculation which is derived from estimated start-up costs, clinical trial costs based on the number of patients and length of treatment and clinical study report costs. These services are performed by the Company's third-party clinical research organizations, laboratories and clinical investigative sites. The expense is recorded in research and development expense each period. Amounts that have been prepaid in advance of work performed are recorded in other current assets.

Stock-Based Compensation — The Company records stock-based compensation expense measured using the fair value method. The Company uses the Black-Scholes option valuation model to calculate stock-based compensation at the date of grant. Option pricing models require the input of highly subjective assumptions, including the expected price volatility. The Company's policy is to estimate forfeitures at the grant date and revise, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Changes in these assumptions can materially affect the fair value estimate.

Net Loss Per Share — Basic net loss per common share is computed by dividing net loss attributable to common stockholders for the period by the weighted average number of common shares outstanding during the period. Although there were warrants and stock options outstanding during 2021 and 2020, they were not included in the computation of any diluted per-share amount when a loss exists, as it would be anti-dilutive. Consequently, diluted net loss per share as presented in the financial statements is equal to basic net loss per share for the years 2021 and 2020. The calculation of diluted earnings per share for 2021 did not include 485,908 shares and 429,791 shares issuable pursuant to the exercise of outstanding common stock options and warrants, respectively, as of December 31, 2021 as the effect would be anti-dilutive. The calculation of diluted earnings per share for 2020 did not include 274,008 shares and 858,699 shares issuable pursuant to the exercise of outstanding common stock options and warrants, respectively, as of December 31, 2020 as the effect would be anti-dilutive.

Use of Estimates — The preparation of consolidated financial statements in conformity with generally accepted accounting principles in the United States ("U.S.") requires management to make estimates and assumptions that affect the amounts reported in the Company's consolidated financial statements and accompanying notes. On an ongoing basis, the Company evaluates its estimates and judgments, which are based on historical and anticipated results and trends as well as on various other assumptions that the Company believes to be reasonable under the circumstances. By their nature, estimates are subject to an inherent degree of uncertainty and, as such, actual results may differ from the Company's estimates. These estimates include accrued clinical trial costs, stock-based compensation expense, valuation of warrants and valuation of deferred tax assets.

Income Taxes — Deferred income tax assets and liabilities are determined based upon differences between the financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

Liquidity — Since its inception, the Company has devoted substantially all of its efforts to product development, raising capital and building infrastructure, and has not generated significant revenues from its planned principal operations. The Company does not anticipate generating significant revenues for the foreseeable future. The Company's activities are subject to significant risks and uncertainties.

The Company has experienced significant losses since its inception, including net losses of $10.4 million and $10.9 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, the Company had an accumulated deficit of $77.7 million and $23.8 million in cash and cash equivalents. The Company has no debt commitments. Substantially all of the Company's net losses have resulted from costs incurred in connection with its research and development activities and its general and administrative expenses to support operations. The Company's net losses may fluctuate significantly from quarter to quarter and year to year.

The Company believes that its available cash at December 31, 2021 will be sufficient to fund liquidity and capital expenditure requirements for at least the next 12 months from the date of issuance of these consolidated financial statements. However, the Company expects to continue to incur significant operating expenses for the foreseeable future in connection with its ongoing activities, including conducting clinical trials, manufacturing development and seeking regulatory approval of its drug candidates, prexigebersen, prexigebersen-A, BP1002 and BP1003. Accordingly, the Company will continue to require substantial additional capital to fund its projected operating requirements. Such additional capital may not be available when needed or on terms favorable to the Company. In addition, the Company may seek additional capital due to favorable market conditions or strategic considerations, even if it believes it has sufficient funds for its current and future operating plan. There can be no assurance that the Company will be able to continue to raise additional capital through the sale of securities in the future. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers and/or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations, financial condition and future prospects.

Recent Accounting Pronouncements — From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (FASB) that are adopted by the Company as of the specified effective date. There are no recent accounting pronouncements that have a material impact on the Company's consolidated financial statements.

3. Prepaid Drug Product

Advance payments, including nonrefundable amounts, for goods or services that will be used or rendered for future clinical development activities are deferred and capitalized. Such amounts will be recognized as an expense as the related goods are delivered or the related services are performed. The Company recognized certain expenses and incurred installment costs for its contract drug manufacturing and raw material suppliers with prepayments totaling $1.3 million as of December 31, 2020 pursuant to drug supply contracts for the manufacture and delivery of prexigebersen for testing in a Phase 2 clinical trial, prexigebersen-A for testing in a Phase 1 clinical trial and BP1002 for testing in a Phase 1 clinical trial. The Company recognized certain expenses and incurred additional installment costs during 2021, with advanced payments remaining to be expensed totaling $0.5 million as of December 31, 2021.

4. Other Current Assets

As of December 31, 2021, other current assets included prepaid expenses of $1.8 million, comprised primarily of prepayments of $1.4 million made for the Company's clinical trials for BP1002 in AML and lymphoma, prexigebersen in AML and prexigebersen-A in solid tumors as well as prepaid insurance of $0.3 million and other prepaid expenses of $0.1 million. As of December 31, 2020, other current assets included prepaid expenses of $0.9 million, comprised primarily of prepayments of $0.6 million made for the Company's clinical trials for BP1002 in lymphoma and prexigebersen-A in solid tumors as well as prepaid insurance of $0.3 million.

5. Property and Equipment

The following table summarizes property and equipment as of December 31, 2021 and 2020:

	Estimated Useful Lives	December 31, 2021	December 31, 2020
	(in years)	(in thousands)	
Leasehold improvements	2 to 5	$ 463	$ 463
Computers and office equipment	3	83	60
Furniture and fixtures	7	93	46
Scientific equipment	7	460	460
Total		1,099	1,029
Less: Accumulated depreciation		(874)	(798)
Net property and equipment		$ 225	$ 231

6. Accounts Payable

As of December 31, 2021, current liabilities included accounts payable of $0.1 million, comprised primarily of legal and patent fees and expenses related to manufacturing totaling $0.1 million. As of December 31, 2020, current liabilities included accounts payable of $0.1 million, comprised primarily of investor relations expenses and legal and patent fees of $0.1 million.

7. Accrued Expense

As of December 31, 2021, current liabilities included accrued expenses of $0.8 million, comprised primarily of accrued employee vacation and bonus expenses of $0.4 million, franchise tax expense of $0.1 million, legal and patent fees of $0.1 million, manufacturing expenses of $0.1 million and other accrued expenses of $0.1 million. As of December 31, 2020, current liabilities included accrued expenses of $1.0 million, comprised primarily of expenses related to the Company's clinical trial for prexigebersen in AML of $0.4 million, accrued employee vacation and bonus expenses of $0.4 million, manufacturing expenses of $0.1 million and other accrued expenses of $0.1 million.

8. Stockholders' Equity

Issuances of Common Stock – On February 16, 2021, the Company entered into a placement agency agreement with Roth Capital Partners, LLC relating to a public offering of 1,710,600 shares of its common stock for gross proceeds of approximately $13.0 million under the 2019 Shelf Registration Statement (the "2021 Public Offering"). In addition, on February 16, 2021, the Company entered into a securities purchase agreement with certain institutional investors pursuant to which it agreed to sell an aggregate of 1,650,000 shares of its common stock in the 2021 Public Offering to such investors. The 2021 Public Offering closed on February 18, 2021. The net proceeds from the 2021 Public Offering, after deducting the placement agent's fees and expenses and the Company's offering expenses, were approximately $12.2 million.

During the year ended December 31, 2021, the Company issued an aggregate of 428,907 shares of its common stock pursuant to the exercise of warrants at a weighted average exercise price of approximately $9.71 per share. The net proceeds to the Company from the exercise of the warrants were approximately $4.2 million. The Company did not issue any common stock pursuant to the exercise of warrants during the year ended December 31, 2020.

At-The-Market Offering Agreement - On July 13, 2020, the Company entered into an At-The-Market Offering Agreement (the "Offering Agreement") with H. C. Wainwright & Co., LLC ("Wainwright"), as sales agent and/or principal, pursuant to which the Company may offer and sell, from time to time, through or to Wainwright, shares of the Company's common stock. Sales of shares of common stock under the Offering Agreement were previously made pursuant to the 2019 Shelf Registration Statement and a related prospectus supplement filed with the SEC on July 14, 2020, for an aggregate offering price of up to $7.0 million. From and after August 18, 2021, sales of shares of common stock under the Offering Agreement will be made pursuant to the 2019 Shelf Registration Statement and a related prospectus supplement filed with the SEC on August 18, 2021, for an aggregate offering price of up to $10.0

million, provided that the Company may be limited in the amount of securities that it can sell under the Offering Agreement pursuant to Instruction I.B.6 to Form S-3 for so long as the Company's public float remains less than $75.0 million. Under the Offering Agreement, Wainwright may sell shares by any method deemed to be an "at the market" offering as defined in Rule 415 under the Securities Act. The Company will pay Wainwright a commission of 3% of the aggregate gross proceeds from each sale of shares under the Offering Agreement and has agreed to provide Wainwright with customary indemnification and contribution rights. The Company has also agreed to reimburse Wainwright for certain specified expenses. During the year ended December 31, 2021, the Company offered and sold 478,800 shares of its common stock under the Offering Agreement for net proceeds of approximately $3.7 million. As of December 31, 2021, the Company had offered and sold 1,328,800 shares of its common stock under the Offering Agreement for gross proceeds of approximately $8.4 million. The net proceeds from the offering, after deducting commissions and offering expenses, were approximately $8.0 million.

Stockholders' Equity totaled $25.5 million as of December 31, 2021 compared to $15.1 million as of December 31, 2020. There were 7,160,164 shares of common stock issued and outstanding as of December 31, 2021. There were no shares of preferred stock issued and outstanding as of December 31, 2021.

9. Stock-Based Compensation Plan

The 2017 Plan – On December 21, 2017, the Company's stockholders approved the Bio-Path Holdings, Inc. 2017 Stock Incentive Plan (as amended, the "2017 Plan"), which replaced the First Amended 2007 Stock Incentive Plan, as amended (the "2007 Plan"). The 2007 Plan expired by its terms in January 2018, and no awards were made under the 2007 Plan from the approval of the 2017 Plan on December 21, 2017 until the expiration of the 2007 Plan. The 2017 Plan provides for the grant of Incentive Stock Options, Non-Qualified Stock Options, Restricted Shares, Restricted Share Units, Stock Appreciation Rights, Performance-Based Awards and other stock-based awards, or any combination of the foregoing to the Company's employees, non-employee directors and consultants. On December 19, 2019, the Company's stockholders approved an amendment to the 2017 Plan to increase the number of shares reserved for grant and issuance pursuant to the 2017 Plan by 600,000 shares to 660,000 shares. As of December 31, 2021, there were 190,224 shares of common stock reserved for future issuance of awards under the 2017 Plan. Under the 2017 Plan, the exercise price of awards is determined by the Board of Directors or the compensation committee of the Board of Directors, and for options intended to qualify as qualified Incentive Stock Options, may not be less than the fair market value as determined by the closing stock price at the date of the grant. Each option and award under the 2017 Plan shall vest and expire as determined by the Board of Directors or the compensation committee. Options expire no later than ten years from the date of grant. All grants provide for accelerated vesting if there is a change of control, as defined in the 2017 Plan.

Stock option awards granted for the years 2021 and 2020 were estimated to have a weighted average fair value per share of $6.22 and $4.34, respectively. The fair value calculation is based on stock options granted during the year using the Black-Scholes option-pricing model on the date of grant. In addition, for all stock options granted, exercise price was determined based on the fair value as determined by the closing stock price at the date of the grant. For stock options granted during 2021 and 2020 the following weighted average assumptions were used in determining fair value:

	2021	2020
Risk-free interest rate	1.15 %	0.50 %
Expected volatility	128 %	122 %
Expected term in years	6.0	6.0
Dividend yield	— %	— %

The Company determines the expected term of its stock option awards using the simplified method based on the weighted average of the length of the vesting period and the term of the exercise period. Expected volatility is determined by the volatility of the Company's historical stock price over the expected term of the grant. The risk-free interest rate for the expected term of each option granted is based on the U.S. Treasury yield curve in effect at the time of grant.

Option activity under the Plans for the year ended December 31, 2021 was as follows (in thousands, except as noted):

	Options (in thousands)	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2020	274	$ 20.57	8.7	$ 3,750
Granted	213	7.02	9.3	
Expired	(1)	72.67		
Outstanding at December 31, 2021	486	$ 14.58	8.4	$ 7,800
Vested and expected to vest December 31, 2021	451	$ 15.21	8.4	$ 7,114
Exercisable at December 31, 2021	178	$ 28.09	7.6	$ 3,412

The aggregate intrinsic value represents the total pretax intrinsic value (the difference between the Company's closing stock price on December 31, 2021 and the exercise price, multiplied by the number of in-the-money options) that would have been received by the option holders had all option holders exercised their options on December 31, 2021. This amount changes based on the fair value of the Company's stock.

Option activity under the Plans for the year ended December 31, 2020 was as follows (in thousands, except as noted):

	Options (in thousands)	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2019	68	$ 68.56	7.7	$ —
Granted	211	5.01	9.4	
Forfeited	(4)	7.19		
Expired	(1)	28.67		
Outstanding at December 31, 2020	274	$ 20.57	8.7	$ 3,750
Vested and expected to vest December 31, 2020	238	$ 22.66	8.7	$ —
Exercisable at December 31, 2020	66	$ 63.95	7.2	$ 3,070

The aggregate intrinsic value represents the total pretax intrinsic value (the difference between the Company's closing stock price on December 31, 2020 and the exercise price, multiplied by the number of in-the-money options) that would have been received by the option holders had all option holders exercised their options on December 31, 2020. This amount changes based on the fair value of the Company's stock.

Stock-Based Compensation Expense – Total stock-based compensation expense for the year ended 2021 was $0.8 million, which consisted of research and development expense of $0.2 million and general and administrative expense of $0.7 million. As of December 31, 2021, future stock-based compensation expense for all outstanding unvested options was $1.4 million, which is expected to be recognized over a weighted-average vesting period of 2.5 years. Total stock-based compensation expense for the year ended 2020 was $0.6 million, which consisted of research and development expense of $0.1 million and general and administrative expense of $0.5 million.

10. Warrants

A summary of warrants outstanding and exercisable as of December 31, 2021 is as follows (in thousands, except as noted):

	Warrants Outstanding			Warrants Exercisable	
Year Issued	Number Outstanding	Weighted Average Remaining Contractual Life (in years)	Weighted Average Exercise Price (per share)	Number Exercisable	Weighted Average Exercise Price (per share)
2016	6	—	$ 466.26	6	$ 466.26
2017	23	0.4	118.95	23	118.95
2018	120	2.2	19.20	120	19.20
2019	281	2.8	13.76	281	13.76
	430	2.5	$ 27.61	430	$ 27.61

11. Commitments and Contingencies

Drug Supplier Project Plan – Total commitments for the Company's drug supplier project plan were $3.2 million as of December 31, 2021, comprised of $1.6 million for the manufacture of prexigebersen drug product, $1.2 million for manufacture of the Company's Grb2 drug substance, $0.3 million for manufacturing development and $0.1 million for testing services. The Company expects to incur $2.6 million of these commitments over the next 12 months.

12. Leases

In April 2014, the Company entered into a five-year lease agreement for administrative office space located in Bellaire, Texas. The term of the lease began on August 1, 2014 and was set to expire on July 31, 2019; however, in May 2019, the Company entered into an amendment to the lease agreement to extend the term of the lease for a period of five years, beginning on August 1, 2019 and ending on October 31, 2024.

In April 2016, the Company entered into a three-year lease agreement for lab space located in Bellaire, Texas. The term of lease began on May 1, 2016 and was set to expire on April 30, 2019; however, in December 2018, the Company entered into an amendment to the lease agreement to extend the term for a period of three years, beginning on May 1, 2019 and ending on April 30, 2022.

At the inception of an agreement, the Company determines if the agreement is a lease based on the unique facts and circumstances in each agreement. Lease classification, recognition, and measurement are then determined at the lease commencement date. For agreements that contain a lease, the Company identifies lease and non-lease components, determines the consideration in the contract, determines whether the lease is an operating or financing lease and recognizes right of use ("ROU") assets and lease liabilities. Lease liabilities and their corresponding ROU assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable so the Company uses an incremental borrowing rate based on the information available at the lease commencement date, which represents an estimated rate that would be incurred to borrow over a similar term in a similar economic environment. The weighted average incremental borrowing rate utilized on its lease liabilities as of December 31, 2021 was 8.0%.

The Company's current leases include options to renew which can impact the lease term. The exercise of these options is at its discretion and the Company does not include any of these options within the expected lease term as there is no reasonable certainty these options will be exercised. Fixed lease payments on operating leases are recognized over the expected term of the lease on a straight-line basis within its consolidated financial statements. The Company's leases are included in ROU assets, current portion of lease liabilities and noncurrent lease liabilities in its consolidated balance sheet for the year ended December 31, 2021.

The following table summarizes the Company's operating lease assets and liabilities:

	December 31,	
	2021	2020
	(in thousands)	
Assets:		
Operating lease assets	$ 203	$ 288
Liabilities:		
Current portion of lease liabilities	82	94
Noncurrent lease liabilities	153	236
Total operating lease liabilities	$ 235	$ 330

The following table summarizes the Company's lease related costs:

	December 31,	
	2021	2020
	(in thousands)	
Operating lease costs	$ 117	$ 115
Variable lease costs	11	6
Total lease costs	$ 128	$ 121

The Company made cash payments for its operating leases of $0.1 million for the year ended December 31, 2021.

The following table summarizes the Company's expected minimum lease payments:

	As of December 31, 2021
	(in thousands)
2022	$ 98
2023	89
2024	76
Future minimum lease payments	263
Less: Interest	(28)
Present value of operating lease liabilities	$ 235

As of December 31, 2021, the weighted average remaining lease term was 2.7 years.

13. Benefit Plan

The Company initiated a contribution savings plan under Section 401(k) of the Internal Revenue Code in 2016. Under the plan, all eligible employees may contribute up to the statutory allowable amount governed by the Internal Revenue Service for any calendar year. The Company makes matching contributions equal to 100% of the first 3% and 50% of the next 2% of each employee's base salary up to the allowable amount, which is fully vested on the date the matching contributions are made. For the years ended December 31, 2021 and 2020, matching contributions totaled $39,000 and $30,000, respectively.

14. Income Taxes

At December 31, 2021, the Company had a net operating loss carryforward for federal income tax purposes of $71.3 million, $35.8 million of which begins to expire in varying amounts in tax year 2026. Approximately $35.5 million of net operating losses, incurred after December 31, 2017, carryforward indefinitely. During each of the years ended December 31, 2021 and 2020, the Company raised additional equity capital. IRC Section 382 imposes certain limitations on the use of net operating losses and research and development tax credits to offset future taxable income when an ownership change has occurred. The Company has yet to determine whether an ownership change occurred in 2021 or 2020. If an ownership change is determined to have occurred, additional limitations on the Company's net operating losses incurred prior to the ownership change may apply. The Company has a research and

development tax credit carryforward of $3.4 million for federal income tax purposes that begins to expire in varying amounts in tax year 2028.

In assessing the ability to realize its 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 ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Management considers evidence such as the reversal of deferred tax liabilities, projected future results of operations, and tax planning strategies in making this assessment. Based upon the level of historical taxable income, significant book losses during the current and prior periods, and projections for future results of operations over the periods in which the deferred tax assets are deductible, among other factors, management continues to conclude that the Company does not meet the "more likely than not" requirement of ASC 740 in order to recognize deferred tax assets. As such, a valuation allowance has been recorded to offset the Company's net deferred tax assets at December 31, 2021. The Company recorded an increase in the valuation allowance of $2.6 million for the year ended December 31, 2021.

Due to the uncertainty surrounding the realization of the benefits of its deferred assets, including NOL carryforwards, the Company has provided a 100% valuation allowance on its deferred tax assets at December 31, 2021 and 2020. The valuation allowance was $19.0 million and $16.4 million as of December 31, 2021 and 2020, respectively.

The components of the Company's deferred tax asset are as follows:

	December 31,	
	2021	2020
	(in thousands)	
Deferred tax assets – non-current		
Accrued bonuses	$ 63	$ 53
Accrued vacation	26	24
Net operating loss (NOL) carryover	14,975	12,876
Research & development tax credits	3,353	2,902
Share based expense	572	472
Other	4	4
Right of use lease liability	49	69
Fixed asset depreciation	43	55
Total deferred tax asset	19,085	16,455
Less: valuation allowance	(19,042)	(16,395)
Net deferred tax asset	43	60
Right of use asset	(43)	(60)
Net deferred tax asset	$ —	$ —

Reconciliation between income taxes at the statutory tax rate (21%) and the actual income tax provision for continuing operations follows:

	December 31,	
	2021	2020
	(in thousands)	
Loss before income taxes	$ (10,440)	$ (10,882)
Tax (benefit) at statutory tax rate	(2,193)	(2,285)
Effects of:		
Exclusion of incentive stock option expense	73	50
R&D tax credits	(451)	(832)
Increase (decrease) in valuation allowance	2,648	2,990
Other	(77)	77
Provision for income taxes	$ —	$ —

As of December 31, 2021, the Company had no unrecognized income tax benefits. The Company's policy for classifying interest and penalties associated with unrecognized income tax benefits is to include such items as tax expense. No interest or penalties have been recorded as of the year ended December 31, 2021, and no interest or penalties have been accrued as of December 31, 2021 and 2020, respectively.

The Company's open years for Internal Revenue Service (IRS) examination purposes due to normal statute of limitation are 2018, 2019 and 2020. However, since the Company has operating loss carryforwards, the IRS has the ability to make adjustments to items that originate in a year otherwise barred by the statute of limitations under Section 6501 of the Internal Revenue Code of 1986, as amended, in order to redetermine tax for an open year to which those items are carried. Therefore, in a year in which a net operating loss deduction was claimed, the IRS may examine the year in which the net operating loss was generated and adjust it accordingly for purposes of assessing additional tax in the year the net operating loss was claimed. The Company is not currently under examination by the IRS or any other taxing authorities.

15. Subsequent Events

In January 2022, the Company exercised an option for its lab space in the lease agreement amendment as described in Note 12 to extend the term of the lease to April 30, 2025.

XBRL-Only Content Section:

Element	Value	
dei:EntityCentralIndexKey#	0001133818	
dei:CurrentFiscalYearEndDate	--12-31	
dei:DocumentFiscalYearFocus	2021	
Dei:DocumentFiscalPeriodFocus	FY	
dei:AmendmentFlag	true/false	