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

FORM 10-K

(Mark One)
☒ Annual Report Under Section 13 Or 15(d) Of The Securities Exchange Act Of 1934

For the fiscal year ended **December 31, 2021**

or

☐ Transition Report Under Section 13 Or 15(d) Of The Securities Exchange Act Of 1934

For the transition period from _____ to _____

COMMISSION FILE NUMBER: 000-52446

ACTINIUM PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**74-2963609**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

275 Madison Avenue, 7th Fl.
New York, NY 10016
(Address of principal executive offices) (Zip Code)

(646) 677-3870
Registrant's telephone number, including area code

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

Title of each class	Trading symbol	Name of exchange on which registered
Common stock, par value $0.001	**ATNM**	**NYSE American**

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

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

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

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

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

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

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

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

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

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

The aggregate market value of voting stock held by nonaffiliates of the registrant as of June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, based on the closing price of the common stock on the NYSE American on June 30, 2021 was $138,622,140.

As of March 25, 2022, 22,143,974 shares of common stock, $0.001 par value per share, were outstanding.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this "Report") contains forward-looking statements that involve risks and uncertainties, principally in the sections entitled "Description of Business," "Risk Factors," and "Management's Discussion and Analysis of Financial Condition and Results of Operations." All statements other than statements of historical fact contained in this Report, including statements regarding future events, our future financial performance, business strategy and plans and objectives of management for future operations, are forward-looking statements. We have attempted to identify forward-looking statements by terminology including "anticipates," "believes," "can," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "should," or "will" or the negative of these terms or other comparable terminology. Although we do not make forward-looking statements unless we believe we have a reasonable basis for doing so, we cannot guarantee their accuracy. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under "Risk Factors" or elsewhere in this Report, which may cause our or our industry's actual results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time and it is not possible for us to predict all risk factors, nor can we address the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause our actual results to differ materially from those contained in any forward-looking statements. All forward-looking statements included in this document are based on information available to us on the date hereof, and we assume no obligation to update any such forward-looking statements.

You should not place undue reliance on any forward-looking statement, each of which applies only as of the date of this Report. Before you invest in our securities, you should be aware that the occurrence of the events described in the section entitled "Risk Factors" and elsewhere in this Report could negatively affect our business, operating results, financial condition and stock price. Except as required by law, we undertake no obligation to update or revise publicly any of the forward-looking statements after the date of this Report to conform our statements to actual results or changed expectations.

PART I

Item 1. BUSINESS.

Business Overview

Actinium Pharmaceuticals, Inc. is a clinical-stage, biopharmaceutical company applying its proprietary platform technology and deep understanding of radiobiology to the development of novel targeted radiotherapies for patients with unmet needs. Our targeted radiotherapies combine the cell-killing ability of radiation via a radioisotope payload with a targeting agent, such as a monoclonal antibody, to deliver radiation in a precise manner inside the body to specific, targeted cells, to potentially achieve greater efficacy with lower toxicity than with external beam radiation. They also enable a broader usage of radiation than external beam radiation as they can be used in the treatment of both solid tumors and blood cancers, which generally cannot be treated with external radiation given their diffuse nature. Our clinical pipeline is focused on targeting the antigens CD45 and CD33, both of which are expressed in multiple hematologic cancers, which are known to be highly sensitive to radiation. Our clinical programs are focused on two primary areas: (1) targeted conditioning prior to a bone marrow transplant ("BMT"), adoptive cell therapy ("ACT") such as CAR-T or gene therapy with Iomab-B and (2) targeted radiotherapy combinations with Actimab-A and other therapeutic agents. Our product development strategy is actively informed by clinical data with Iomab-B and Actimab-A in approximately 600 patients, including our ongoing Pivotal Phase 3 SIERRA trial, which completed its targeted enrollment of 150 patients in the third quarter of 2021, with the last patient receiving their BMT in the fourth quarter of 2021. Our clinical pipeline has emanated from our Antibody Warhead Enabling ("AWE") technology platform, which is protected by over 170 issued and pending patents, trade secrets and know-how that we are applying to the development of targeted radiotherapies for blood and solid tumor indications, independently and with collaborators. Ongoing collaborations include a research partnership with Astellas Pharma, Inc. ("Astellas") focused on the development of theranostics, which enable the diagnosis and treatment, for solid tumor indications, a collaboration with EpicentRx, Inc, focused on a novel CD47 immunotherapy targeted radiotherapy combination, leveraging EpicentRx's RRx-01, that is being studied in a Phase 3 trial in non-small cell lung cancer, with our clinical stage Actimab-A in AML models, and a collaboration with AVEO Oncology, focused on developing a HER3 targeting ARC or Antibody Radiation Conjugate for solid tumors leveraging with their clinical stage antibody. We are also utilizing our AWE technology platform to advance our research objectives focused on developing next-generation targeted radiotherapies with our expanded research and development organization and research laboratories leveraging our drug development experience.

Targeted Conditioning

To the best of our knowledge, we are advancing the only multi-target, multi-indication, clinical-stage pipeline for targeted conditioning. Our targeted conditioning agents are intended to potentially enable improved access and outcomes to cell-based therapies with curative potential, including BMT, ACT, and gene therapy Conditioning in the context of BMT, ACT or gene therapy is the act of depleting certain blood and immune-forming cells, including bone marrow stem cells and, in some cases, cancer cells prior to transplanting new cells into a patient. Currently, conditioning is accomplished using a combination of cytotoxic chemotherapeutic agents and external radiation. These non-targeted conditioning regimens are highly toxic and may prevent a patient from receiving a potentially curative therapy and hinder outcomes. We believe our targeted conditioning agents have the potential to increase patient access and outcomes by way of their ability to selectively deplete targeted cells while sparing normal healthy cells, resulting in potentially lower systemic and off-target toxicities. We use our ARCs both at high isotope dose levels to achieve myeloablation, which fully depletes bone marrow stem cells and at lower isotope dose levels to achieve lymphodepletion, which spares bone marrow stem cells from depletion. In addition, dosing may be titrated downward from myeloablative doses to achieve partial myeloablation, which may be appropriate for certain gene therapy programs.

CD45 Targeted Conditioning Program

Iomab-B (I-131 apamistamab), our lead candidate and targeted conditioning agent is comprised of the anti-CD45 monoclonal antibody known as apamistamab (formerly BC8) and the radioisotope Iodine-131 ("I-131"). CD45 is an antigen expressed on leukemia, lymphoma and myeloma cancer cells, as well as nucleated immune cells including bone marrow stem cells, but is not expressed outside of the hematopoietic, or blood forming, system. This unique expression on blood cancer and immune cells enables simultaneous depletion of both cell types, making CD45 an optimal antigen for targeted conditioning applications. CD45 is a cell surface antigen with an average expression of 200,000 copies per cell, however, it only internalizes at a rate of 10-15%. We believe our ARC approach is the most effective method to target CD45 positive cells, as the radioisotope payload linear energy transfer can readily ablate a targeted cell without requiring payload internalization like an antibody drug conjugate or without relying on biological effector function processes like a naked antibody. Furthermore, since CD45 expression level varies from low to high antigen density as the immune cells become more terminally differentiated, we can selectively condition depending on the therapeutic application, from full myeloablation to transient lymphodepletion, by adjusting the dose or intensity of the I-131 isotope payload. Full myeloablation can be achieved with high doses of I-131, as its energy pathlength and crossfire effect can penetrate into bone marrow niches to target and deplete blood and immune system forming bone marrow stem cells. Myeloablation is applicable to autologous or allogeneic BMT and to autologous gene-edited or modified therapies that can reconstitute a patient's blood and immune systems. Alternatively, low doses of I-131 can be transiently lymphodepleting and spare a patient's bone marrow stem cells, which we believe is ideal for ACT applications such as CAR-T. We intend to develop our CD45 targeted conditioning program for BMT, ACT and gene therapy applications for malignant and non-malignant diseases and believe that multiple radioisotopes beyond I-131 may be utilized including alpha and beta emitters.

Iomab-B uses high doses of I-131 to achieve myeloablative conditioning prior to a BMT, is currently being studied in the pivotal Phase 3 Study of Iomab-B in Elderly Relapsed or Refractory AML ("SIERRA"), clinical trial for targeted conditioning prior to an allogeneic BMT for patients with active, relapsed or refractory ("r/r") Acute Myeloid Leukemia, ("AML"), who are age 55 or older. Enrollment of the planned 150 patients in the SIERRA trial was completed in the third quarter of 2021 with the last patient receiving their BMT in the fourth quarter of 2021. Patients with active, r/r AML are not normally considered eligible for BMT and the SIERRA trial is the only randomized Phase 3 trial to offer BMT as a treatment option for this patient population. The SIERRA trial compares outcomes of patients randomized to receive Iomab-B and a BMT (the "study arm") to those patients randomized to receive physician's choice of salvage therapy (the "control arm"). The control arm is also defined as conventional care, as no standard of care exists for this patient population and includes over 20 agents that may be used as single agents or in combination including venetoclax, a targeted Bcl-2 inhibitor, Midostaurin and Sorafenib, targeted FLT3 inhibitors, hypomethylating agents and cytotoxic chemotherapies. Patients who fail to achieve a Complete Remission ("CR") on the control arm are ineligible to proceed to a BMT, but the trial design permits these patients to "cross over" to receive the study arm treatment if they meet the eligibility criteria. The primary endpoint of the SIERRA trial is durable Complete Remission ("dCR") of 180 days and the secondary endpoint is Overall Survival ("OS"). When the crossover patients receive Iomab-B and BMT, they have not achieved remission with their salvage therapy and are considered to be failures for the primary endpoint of the study. The SIERRA trial recruited patients at 24 sites in the United States and Canada, which includes many of the leading BMT sites based on volume. If approved, we expect our initial commercial launch would target the leading 50-100 BMT and medical centers that perform the vast majority of BMT's in the United States. In the European Union ("EU"), we received favorable feedback from the European Medicines Agency ("EMA") via their scientific advice program that the trial design, primary endpoint and planned statistical analysis from the SIERRA trial are acceptable as the basis for a Marketing Authorization Application, or MAA. Additionally, the EMA commented that it does not anticipate the need for further standalone preclinical toxicology or safety studies. Overall, transplant procedures in the EU are approximately fifty percent higher than in the United States with a similar market dynamic, with a majority of BMT volume being conducted in a concentrated number of leading medical centers. Currently we intend to secure a partner for Iomab-B in the EU.

Data from full patient enrollment in the SIERRA trial (151 patients), was presented at the American Society of Hematology ("ASH") Annual Meeting in December 2021. The data presented includes rates of BMT access and engraftment, 100-day non-relapse transplant-related mortality (100-day TRM) and adverse events, which has been reported from interim analyses conducted at 25%, 50% 75% and 100% of patient enrollment pursuant to the study protocol. The data presented at ASH highlighted that 100% of patients (59/59) on the study arm that received a therapeutic dose of Iomab-B received a BMT, with a median time to BMT of 30 days, and all patients achieved neutrophil and platelet engraftment in a median time of 18 days despite a high median blast count of 29%. On the control arm, only 17% of patients (13/76) achieved remission after salvage therapy, and then received a BMT with a median time to BMT of 67 days and median blast count of 20%. Of the 83% of patients failing to achieve a CR with conventional care (47/57), 30 patients were eligible to cross over to receive Iomab-B followed by transplant. These patients are considered as having failed the primary endpoint of the study. All crossover patients who received the therapeutic dose of Iomab-B (30/30) received a BMT, with a median time to BMT of 24 days and they achieved engraftment in a median time of 19 days despite high median blast count of 22% at time of crossover. It was also reported that 100-day TRM of the study or Iomab-B arm was 10% (6/59) of patients that received a BMT compared to 15% of patients (2/13) who received a BMT after salvage therapy on the control arm. The universal engraftment rate and low 100-day TRM rate of the Iomab-B arm resulted in 53 patients potentially evaluable for the primary endpoint compared to 11 patients in the control arm, an approximate five times difference. At each of the interim analyses throughout the SIERRA trial, this approximate five times difference has been consistent in favor of the Iomab-B arm as a result of higher rates of BMT engraftment and lower rates of 100-day TRM.

Data from the SIERRA trial has also been accepted for presentation at the upcoming Transplantation & Cellular Therapy ("TCT") Tandem Meetings of the American Society for Transplantation and Cellular Therapy ("ASTCT") and Center for International Bone & Marrow Transplant Research ("CIBMTR"), which has been postponed from February to April 2022. At TCT, we expect to present additional data from the SIERRA trial to include patients who have matured for BMT engraftment and 100-day TRM analysis, for which data was not available at time of the submission cutoff for ASH in December of 2021. Top-line data for the primary endpoint of durable Complete Remission is expected to be presented in the third quarter of 2022. We believe topline data from SIERRA will support the submission of a Biologics License Application ("BLA") with the U.S. Food and Drug Administration ("FDA"), which we expect to file in the first half of 2023.

Our Iomab-ACT program is intended for targeted conditioning prior to ACT or gene therapy and uses the same I-131-apamistamab construct as Iomab-B at varying doses. At lower doses of one-eighth to one-sixth of the myeloablative dose, it is applicable for lymphodepletion prior to CAR-T or certain gene therapy applications where stem cell myeloablation is not necessary. At higher doses it is applicable for gene therapy applications where stem cell myeloablation is necessary.

We believe our Iomab-ACT program is highly differentiated when compared to Fludarabine and Cyclophosphamide ("Flu/Cy") or other chemotherapy-based regimens that are used as the standard of practice today for lymphodepletion prior to CAR-T. CD45 is an antigen expressed on certain immune cell types that are relevant to the mechanism of CAR-T therapies including lymphocytes, regulatory T-cells and macrophages that have been associated with clinical responses that may limit the safety, efficacy and durability of response of these CAR-T therapies including cytokine release syndrome ("CRS") and neurotoxicity. Some of these limitations may be attributable to the chemotherapy-based conditioning agents that are being used prior to CAR-T therapies. Preclinical data supporting the rational for our Iomab-ACT program was presented at multiple medical conferences in 2019. Unlike chemotherapy, Iomab-ACT is targeted in nature and, due to this CD45-directed targeting, we expect we can improve CAR-T cell expansion, potentially resulting in responses that are more durable, but also resulting in reduced CAR-T related toxicities. Importantly, we expect the Iomab-ACT program construct to enable lymphodepletion through a single-dose, outpatient administration versus Flu/Cy or other chemotherapy-based lymphodepletion regimens that can require multiple infusion cycles over several days. Because of this potentially superior profile, the Iomab-ACT construct could result in improved access to CAR-T therapy and better outcomes.

We are studying Iomab-ACT in a clinical collaboration with Memorial Sloan Kettering Cancer Center ("MSKCC") for targeted conditioning prior to administration of MSKCC's 19-28z CD19 targeting CAR-T in patients with relapsed or refractory B-cell acute lymphoblastic leukemia ("ALL") or diffuse large B-cell lymphoma ("DLBCL"). We received grant funding from the National Institute of Health ("NIH") to fund this trial with MSKCC being a co-recipient on this grant. This is a first of its kind study to use an ARC-based conditioning regimen with CAR-T therapy. The hypothesized rationale for this study is that Iomab-ACT will exert an anti-tumor effect on the chemotherapy-refractory B-ALL cells that are sensitive to radiation resulting in reduced disease burden and simultaneously deplete CD45 expressing immune cells implicated in CAR-T related toxicities, resulting in an optimal homeostatic environment for the CAR-T cells. Results with MSKCC's 19-28z CD-19 CAR-T in 53 patients with r/r B-ALL published in the New England Journal of Medicine reported complete remissions in 83% (44/53) of patients, which compares favorably to standard chemotherapy regimens that have complete remission rates of 18% - 45% in this patient population. Median event-free survival (EFS) was 6.1 months and median overall survival (OS) was 12.9 months at a median follow up period of 29 months (range 1 – 65 months). There was a 26% (14/53) rate of Grade 3 or greater CRS and a 42% rate of Grade 3 or 4 neurotoxicity reported. The study will evaluate the feasibility of using an ARC-based conditioning regimen with CAR-T therapy and will evaluate safety measures including incidence of CRS and neurotoxicity and efficacy measures including responses and survival outcomes. In March 2021, we announced that patient enrollment was initiated, and the first patient was administered Iomab-ACT followed by their 19-28z CAR-T therapy. We expect proof of concept data from this study in the second half of 2022.

In addition, we are working in collaboration with the University of California Davis to utilize Iomab-ACT conditioning with a novel anti-HIV autologous gene therapy. We continue to identify additional gene therapies for which Iomab-ACT can be used for targeted conditioning with the goal of collaborating with multiple academic or industry developers to establish Iomab-ACT as a non-chemotherapy universal targeted conditioning solution.

CD33 Program: Combinations and Therapeutics

Our CD33 program is evaluating the clinical utility of Actimab-A, comprised of the anti-CD33 mAb lintuzumab linked to the potent alpha-emitting radioisotope Actinium-225 ("Ac-225"). CD33 is expressed in the majority of patients with AML and myelodysplastic syndrome ("MDS") as well as approximately one-third of patients with multiple myeloma. Ac-225 emits four alpha particles and can kill a cell with one alpha-particle hit, making it one of the most powerful cell-killing agents with no know resistance mechanism to the double strand DNA breaks it can cause. We source Ac-225 from the Department of Energy's Oak Ridge National Laboratory.

Our CD33 development program is driven by data obtained from nearly one hundred fifty treated patients, including results from a Phase 1/2 trial that studied Actimab-A as a single agent at multiple dose levels in 58 patients with newly diagnosed AML, which was completed in 2018, as well as trials studying Actimab-A in combination with other agents.

We believe that radiation delivered internally via a targeting moiety can be synergistic when used in combination with chemotherapy, targeted agents and immunotherapy based on mechanistic rationales supported by our own clinical data, preclinical research and scientific and clinical evidence in the literature. We have prioritized our efforts and resources in favor of combination trials for our CD33 program development strategy rather than single agent trials at this time as we believe Actimab-A can be a backbone therapy in AML when combined with other therapeutic modalities. Our CD33 development program encompasses the following ongoing trials:

<u>Actimab -A Combination Trials</u>:

Actimab-A + CLAG-M

The combination of Actimab-A with CLAG-M has been studied in a Phase 1 combination trial that was conducted in collaboration with the Medical College of Wisconsin ("MCW") in patients age 18 and above with r/r AML who are fit for intensive therapy. Patient enrollment was completed in November 2021. CLAG-M (cladribine, cytarabine, filgrastim and mitoxantrone) is a salvage chemotherapy regimen that produced a 55% remission rate in patients with r/r AML in a previous study conducted by MCW that compared outcomes of patients receiving either CLAG-M, MEC or CLAG salvage therapy regimens. Data from the Phase 1 combination trial of Actimab-A + CLAG-M were presented at ASH in December 2021. After completion of dose-escalation in the Phase 1 trial, the recommended Phase 2 dose was determined to be 0.75 µCi/kg of Actimab-A. 3 patients were enrolled in the 0.75 µCi/kg dose cohort, which had a 100% remission rate comprised of 1 complete remission ("CR") and 2 complete remissions with incomplete platelet recovery ("CRp"), there were no dose limiting toxicities ("DLTs") or 30-day mortality reported. Overall, a 67% (12/18) overall response rate ("ORR") was reported across all dose cohorts (0.25 – 1.0 µCi/kg) and remissions were achieved in every dose cohort including the 0.25 and 0.50 µCi/kg doses of Actimab-A, which have been shown to be subtherapeutic as a single agent. In addition, there was a 72% minimal residual disease ("MRD") negativity rate, which compares favorably to the 39% MRD negativity rate reported by MCW with CLAG-M alone. This study enrolled patients who previously failed Venetoclax, a targeted Bcl-2 inhibitor, and efficacy was similar in patients Venetoclax naïve and those that previously failed Venetoclax, with a 60% response rate in previous Venetoclax failures. We are working to develop a regulatory and development pathway for the Actimab-A CLAG-M combination and will be evaluating potential registration enabling strategies. In addition, we believe this Actimab-A + CLAG-M combination study has provided proof of principle that the addition of Actimab-A to other AML therapies can lead to well-tolerated regimens with improved responses, which supports our Actimab-A backbone therapy in AML strategy.

Actimab-A + Venetoclax

We are also conducting a Phase 1/2 Actimab-A combination trial with the Bcl-2 inhibitor Venetoclax in fit and unfit patients age 18 and above with relapsed or refractory AML. This multi-center trial is being led by UCLA Medical Center. This combination is supported by mechanistic evidence in preclinical studies using Venetoclax - resistant AML tumor cell lines. In these models, we have demonstrated that Actimab-A can deplete Mcl-1 and Bcl-XL, two proteins implicated in mediating resistance to Venetoclax, in addition to causing potentially lethal double-stranded DNA breaks in these CD33 expressing cells. Furthermore, in vivo studies in animal models of Venetoclax-resistant AML demonstrated robust tumor regression and improved survival in cohorts receiving the Actimab-A Venetoclax combination compared to Venetoclax alone. The rationale for this clinical study is that the addition of Actimab-A will; 1) have a direct anti-tumor effect via double-stranded DNA breaks and 2) deplete Mcl-1 and Bcl-XL making the AML cells more susceptible to Venetoclax. Updated data from the Phase 1 dose escalation portion of this study was presented at ASH in December 2021 from three dose cohorts of 0.50, 0.75 and 1.0 µCi/kg of Actimab-A in a total of 12 patients. 50% of patients received Venetoclax therapy prior to enrollment on the Actimab-A combination trial. And 67% of patients had poor risk cytogenetics, of which, 3 had a TP53 mutation, which is associate with poorer response rates and survival outcomes. Of the patients with a TP53 mutation, 67% achieved a remission including a patient that achieved a CR and at the time of data cutoff for ASH, the patient was in follow-up 230 days (~7.5 months). The combination of Actimab-A with Venetoclax was reported to be well-tolerated with no 30-day mortality. The data to date support advancing to the Phase 2 portion of the trial and we expect to provide an update on the development strategy, including consideration of patients with a TP53 mutation, after the Phase 1 dose finding portion of the trial is complete and the recommended Phase 2 dose is determined.

In addition to these ongoing trials, we actively seek and evaluate additional modalities and agents that can be the basis for Actimab-A therapeutic combinations such as the CD47 immunotherapy magrolimab combinations we announced at the Society for Immunotherapy of Cancer in November 2021 to leverage our clinical experience, supply chain and AWE technology platform.

CD47 Based ARC Combinations in Solid Tumors and Blood Cancers

CD47 is a macrophage checkpoint that is upregulated in multiple cancers including blood cancers such as AML and MDS as well as solid tumors. CD47 acts as a "don't eat me" signal on cancer cells to suppress phagocytosis and evade detection and destruction by the immune system. It has become an immunotherapy target of significant interest with multiple biopharmaceutical companies actively developing CD47 targeting agents across a wide range of oncology and hematology indications. CD47 targeting agents have shown limited efficacy as single agent monotherapies in AML/MDS or solid tumors, which has led to combinations such as with hypomethylating agents in AML/MDS. We hypothesized that targeted radiotherapy via ARCs could synergize with CD47 targeting agents via the direct cytotoxic and immunogenic effect of ARCs without overlapping toxicities. To explore this synergy and the potential to improve patient outcomes and we have initiated a program in AML with our Actimab-A ARC, consistent with our strategy to establish Actimab-A a backbone AML therapy, and in solid tumors with a HER-2 targeting ARC, which emanated from our AWE technology platform. To our knowledge, these are the first and only ARC-based targeted radiotherapy combinations with CD47 immunotherapy. Data from these novel combinations were presented at the 36th Annual Meeting of the Society for Immunotherapy for Cancer.

The most advanced CD47 development programs are being studied in patients with AML and MDS. Leveraging our clinical experience with Actimab-A in these indications we have begun studying Actimab-A with the anti-CD47 antibody immunotherapy magrolimab, which is owned by Gilead Sciences, Inc., in preclinical models of AML. In preclinical models, it was shown that in multiple AML cell lines, the combination of Actimab-A with magrolimab led to increased phagocytosis of AML cells compared to magrolimab alone. Our studies also demonstrated that AML cell lines exposed to Actimab-A had an upregulation of calreticulin, which is a pro-phagocytic or "eat me" signal, which we hypothesize makes Actimab-A potentially synergistic with magrolimab and other anti-CD47 antibodies. The Actimab-A and magrolimab combination showed a significant increase in survival compared to Actimab-A alone in a disseminated AML animal tumor model. We intend to continue to study preclinically this combination with the goal of advancing to human clinical trials.

In January 2022, we announced a research collaboration with EpicentRx that will evaluate Actimab-A in combination with EpicentRx's RRx-001in AML. EpicentRx's RRx-001, currently under investigation in a Phase 3 trial for Small Cell Lung Cancer and in other oncology and non-oncology indications, is a versatile next generation small molecule immunotherapeutic that targets the CD47-SIRPα axis and the NLRP3 inflammasome to alter the tumor microenvironment and optimize immune response. This collaboration will explore the mechanistic synergy of RRx-001's CD47–SIRPα downregulation with Actinium's targeted radiotherapy calreticulin upregulation to increase the immune detection and destruction of cancer cells. Preclinical experiments have begun exploring this combination in AML models. We intend to leverage our experience with CD47 targeting agents such as magrolimab in this collaboration. Based on Actimab-A and RRx-001 both being clinical-stage assets, we believe there is a potentially faster pathway to clinical trials with this novel combination, particularly if the preclinical safety and efficacy profile are in line with what was observed with Actimab-A and magrolimab.

Antibody Warhead Enabling Technology Platform

Our proprietary AWE technology platform is supported by intellectual property, know-how and trade secrets that cover the generation, development, methods of use and manufacture of targeted radiotherapies and certain of their components. Our AWE technology patent portfolio presently includes 39 patent families comprised of 173 issued patents and pending patent applications, of which 8 are issued and 30 are pending in the United States, and 135 are issued or pending internationally. The effective lives of the issued patents in our portfolio, or patents that may issue from the pending applications in our portfolio, ranges from expirations between 2024 and 2042. Our technology enables the direct labeling, or conjugation and labeling, of a biomolecular targeting agent to a radionuclide warhead and its development and use as a therapeutic regimen for the treatment of diseases such as cancer. Our AWE intellectual property covers various methods of use in multiple diseases, including indication, dose and scheduling, radionuclide warhead, and therapeutic combinations. We have particular expertise in utilizing the alpha emitting isotope Ac-225 including clinical experience in treating approximately 150 patients with our alpha-emitter-based therapies, "gold standard" linker technology and 5 issued patents in the United States and 49 patents internationally related to the manufacturing or Ac-225 in a cyclotron, which we believe has the potential to produce higher quantities of Ac-225 than currently utilized methods.

In 2021 we have enhanced our research and development capabilities around AWE by securing and staffing research facilities. Our research laboratories are focused on applying our AWE technology platform to the development of radiation conjugates and to execute on research collaborations. Our R&D efforts employ a multidisciplinary approach leveraging our team's knowledge and experience in cancer cell biology, radiochemistry, radiation sciences, immunology and oncology drug development. We intend to focus on generating targeted radiotherapies using our existing intellectual property, evaluating assets for in-licensing to complement our existing clinical pipeline and securing collaborations and partnerships with biopharmaceutical companies. By adding research and development capabilities to our clinical development and clinical supply chain capabilities, we seek to enable the rapid translation of radiotherapies.

Our AWE technology platform is being utilized in our ongoing research collaboration with Astellas to arm select targeting agents owned by Astellas with the alpha-emitting radioisotope Ac-225 for the development of theranostics for solid tumor indications, which combine the ability of radioisotopes to be used for both diagnostic and therapeutic purposes.

We also utilized AWE to create aHER2-targeting radiotherapy using the antibody Trastuzumab with either Ac-225 or Lu-177 radioisotopes to study in combination with magrolimab for solid tumors. Anti-CD47 monotherapies, such as magrolimab, have not shown meaningful responses in clinical studies in solid tumors. We hypothesized that radiation directed at HER2 expressing cells would upregulate cell surface calreticulin, a pro-phagocytic "eat me" signal, that when combined with an anti-CD47 blockade therapy would enhance antitumor activity. Data from this combination was presented at the Annual Meeting of the Society for Immunotherapy for Cancer in November 2021. In vitro studies showed that immunogenicity, determined by binding to HER2 expressing cells, remained intact after radiolabeling Trastuzumab with Ac-225 or Lu-177. In multiple cells lines radiolabeled Trastuzumab increased cell surface calreticulin and the combination with magrolimab increased phagocytosis. The combination of the Ac-225 or Lu-117 Trastuzumab with magrolimab slowed tumor growth in animal models of solid tumors compared to either the radiolabeled Trastuzumab or magrolimab as single agents. We are continuing to evaluate this combination in additional tumor models, and we intend to continue to study this combination with the goal of advancing to human clinical trials.

We are also collaborating with AVEO Oncology ("AVEO") to develop a targeted radiotherapy against ErbB3, also known as HER3, with the Ac-225 isotope for solid tumor indications. HER3 is overexpressed in several solid tumor indications with high unmet needs, including colorectal, gastric, head and neck, breast, ovarian, melanoma, prostate and bladder cancers with HER3 agents under development demonstrating activity in preclinical and clinical studies. To our knowledge, this is the first HER3 targeting radiotherapy in development. AVEO is developing high affinity antibodies including HER3 targeting AV-203, which has demonstrated preclinical activity across a number of solid tumor indications and was studied in a Phase 1 open-label trial in patients with advanced solid tumors where it was found to be safe and generally well tolerated. In March 2022, we announced that data from studies of Ac-225 radiolabeled HER3 antibody have been accepted for presentation at the American Association for Cancer Research ("AACR") Annual Meeting. Preliminary results contained in the AACR abstract showed potent tumor cell cytotoxicity, complete anti-tumor response in a HER3 tumor xenograft models and significantly prolonged survival compared to control groups ($p<0.0001$). Additional data from these studies will be presented at AACR in April 2022. We believe these preliminary results support our collaboration with AVEO and given that AV-203 has clinical safety data, a potentially accelerated regulatory pathway to clinical studies with an Ac-225 HER3 targeted radiotherapy.

Intellectual Property Portfolio and Regulatory Protections

Intellectual Property

We have developed or in-licensed numerous patents and patent applications and possess substantial know-how and trade secrets related to the development and manufacture of our products. As of March 2022, our patent portfolio includes 39 patent families comprised of 174 issued patents and pending patent applications, of which 8 are issued and 30 are pending in the United States, and 135 are issued or pending internationally. Several non-provisional patent applications are expected to be filed in 2022 based on provisional patent applications filed in 2021. More than 90% of our patents are Actinium-owned and the remainder are in-licensed from third parties. These patents cover key areas of our business, including the use of actinium-225 and other alpha- or beta-emitting isotopes attached to cancer targeting carriers like monoclonal antibodies in the treatment of cancers and non-malignant medical disorders, methods for manufacturing key components of our product candidates including actinium-225, an alpha particle emitting radioisotope and carrier antibodies, or Iodine-131, a beta particle emitting radioisotope, and methods for manufacturing finished product candidates for use in cancer treatment.

We own two issued patents in the United States and issued patents in Europe and Japan that relate to the composition of our Iomab-B product candidate. The basis patent terms of these patents expire in 2036 and 2037. Four related patent applications are also currently pending in the U.S. and internationally. In addition, we own both U.S. and international pending patent applications that relate to the use of Iomab-B or Iomab-ACT in the treatment of cancers and non-malignant conditions. We also own five issued patents in the United States and 49 patents outside the United States that relate to the manufacturing of actinium-225, the radionuclide used in our Actimab-A product candidate, in a cyclotron. These patents will expire in the years 2024 through 2027. In addition, we also own U.S. and international patents and pending patent applications that relate to the manufacturing of Actimab-A and its use in the treatment of cancers.

Regulatory Protections

The indications for which we are developing our product candidates for are orphan drug designations, which are disease indications that affect fewer than 200,000 patients in the United States and less than 5 in 10,000 patients in the EU. We have received orphan drug designation for Iomab-B and Actimab-A for patients with AML in both the United States and the EU. As a result, if our products are to be approved, they may receive 7 years and 10 years of market exclusivity in the United States and EU, respectively. In addition, our product candidates are biologics combined with radioisotopes. We believe that the nature of radioisotopes having half-lives combined with the complexities of biologic drugs would make it difficult for a manufacturer to demonstrate bioequivalence to our product candidates. The Hatch-Waxman Act requires that a manufacturer of generic drugs, for which a biologic drug is called a biosimilar, demonstrate bioequivalence to the innovator. However, we are not aware of any existing or pending regulations or legislation that pertains to generic radiopharmaceutical products such as our antibody radiation-conjugate product candidates

Competition

The biopharmaceutical industry in which we operate, specifically, the field of oncology drug development is rapidly evolving and highly competitive. Radiopharmaceuticals for the treatment of cancer has received considerable interest from major and specialty pharmaceutical companies, biotechnology companies, academic research institutions and other public and private entities, particularly in recent years.

For the targeted radiotherapies we are developing, we face competition from biopharmaceuticals companies who are developing alpha particle-based therapies utilizing Actinium-225, Radium-223 and Thorium-227. Companies developing targeted alpha therapies include Bayer AG, who owns Xofigo, the only approved alpha therapy, that is used in the treatment of metastatic prostate cancer, Novartis AG, Telix Pharmaceuticals Limited, Point Biopharma, Inc., Fusion Pharmaceuticals, Inc., RayzeBio, Inc., Aktis Oncology, Curie Therapeutics, RadioMedix, Inc. and Orano Med. Significant attention and resources is being applied to Ac-225 based therapies given its high linear energy and short path length. Fusion Pharmaceuticals is studying FPI-1434, targeting IFG-1R with Ac-225 in a Phase 1 trial in solid tumors and has recently initiated a Phase 1 study to test FGFR3 targeting agent in development. Point Biopharma is studying PNT2002, a PSMA targeting agent for metastatic prostate cancer in a Phase 1 trial, PNT2004, a preclinical agent targeting solid tumors expressing FAP, and PNT2001, a preclinical agent also targeting PSMA in prostate cancer, which all utilize Ac-225. Novartis is also developing a PSMA targeting agent utilizing Ac-225 for prostate cancer. RayzeBio, Aktis Oncology and Curie Therapeutics are all pursuing Ac-225 based therapies but have not yet disclosed cancer targets or indications.

To our knowledge, our Actimab-A product candidate is the only clinical stage Ac-225 based therapy in active development for hematologic indications.

There are also several companies developing beta particle-based therapies such as Bayer, Novartis, Lantheus Holdings, Inc. and Q BioMed, Inc., who all own approved products. Beta particles used for oncology therapeutics includes Iodine-131, Lutetium-177, Strontium-89 and Yttrium-90. Companies developing beta particle-based therapies includes Cellectar Biosciences, Inc., Clovis Oncology, Inc., Y-mAbs Therapeutics, Inc., Ipsen S.A., and Novartis.

In the field of conditioning, pharmaceuticals currently used for myeloablation prior to a bone marrow transplant, lymphodepletion prior to CAR-T and other adoptive cell therapies and conditioning for gene therapy are largely generic, non-targeted chemotherapeutic agents like fludarabine or busulfan and/or total body irradiation.

In targeted conditioning, we face competition from companies developing agents targeting CD117 (Jasper Therapeutics and Magenta Therapeutics), CD45 (Magenta Therapeutics) and CD66 (Telix Pharmaceuticals). CD117 is expressed in normal CNS, GI, reproductive, kidney and skin tissue, which could result in on-target toxicity to these organs. CD117 is not expressed on mature circulating immune cells and thus cannot be targeted for lymphodepletion for adoptive cell therapy. Jasper Therapeutics, Inc, is developing JSP191, an anti-CD117 unconjugated monoclonal antibody that is being studied in a Phase 1b trial in combination with fludarabine and total body irradiation in patients with MDS and AML. Magenta has initiated a Phase 1/2 trial for its MGTA-117 CD117 ADC and will conduct this first in human dose finding study in patients with r/r AML MDS with excess blasts and is exploring MGTA-117 for gene therapy conditioning in preclinical studies. Magenta is also developing its CD45 ADC, which is has not yet been studied in humans and is being evaluated in IND enabling studies.

Forty Seven, Inc.(acquired by Gilead) announced a conditioning regimen comprised of its anti-CD47 monoclonal antibody Magrolimab with its preclinical stage FSI-174 anti-CD117 monoclonal antibody in a preclinical collaboration with bluebird bio, Inc. for conditioning prior to gene therapy.

Molecular Templates announced a collaboration with Vertex focused on targeted conditioning using its Engineered Toxin Bodies (ETBs) with two targets that were not disclosed. In October 2021, Vertex terminated the research collaboration with Molecular Templates. Molecular Templates has a preclinical stage CD45 ETB in development.

Telix Pharmaceuticals is developing TLX66, a CD66 targeting antibody radio conjugated with Yttrium-90, for BMT conditioning in patients with Systemic Amyloid Light-Chain Amyloidosis (SALA). TLX66 is also being studied in a Phase 2 investigator sponsored trial in the U.K in patients with childhood leukemia.

Allogene Therapeutics is developing an anti-CD52 monoclonal antibody for use as a lymphodepletion agent in conjunction with CAR-T therapies. CD52 is not expressed on stem cells and therefore cannot be used for myeloablation for a bone marrow transplant.

To our knowledge, we are the only company with an anti-CD45 radio conjugate in clinical development and the only company with a targeted conditioning agent that has completed enrollment of a pivotal Phase 3 trial.

Our Actimab-A product candidate faces competition from several major pharmaceutical companies and biotechnology companies who are also developing multiple types of therapies including chemotherapy, targeted agents, ADCs, monoclonal antibodies, bispecific antibodies, immunotherapies and cellular therapies for patients with AML. The standard of care for patients with AML has long been “7+3”, which is 7 days of treatment with cytarabine with an anthracycline on the first 3 days for patients who can tolerate intensive therapy and hypomethylating agents, azacitidine or decitabine, for patients who are “unfit” and cannot tolerate intensive therapy. Since 2017, 9 agents have been approved for patients with AML. These approved agents include Vyxeos (liposomal cytarabine and daunorubicin) owned by Jazz Pharmaceuticals, venetoclax, a Bcl-2 inhibitor owned by Abbvie, FLT3 inhibitors midostaurin (owned by Novartis) and gilteritinib (owned by Astellas), Daurismo, a hedgehog pathway inhibitor owned by Pfizer, IDH inhibitors Tibsovo (IDH1) and Idhifa (IDH2) owned by Servier, Onureg (oral azacitidine) owned by Bristol Myers Squibb and Mylotarg, a CD33 targeting ADC owned by Pfizer.

These agents are approved in various AML patient segments including secondary or treatment related AML (Vyxeos), patients over the age of 75 or patients unfit for intensive therapy (venetoclax and Daurismo) and patients with a specific cytogenetic mutation such as FLT3 or IDH1/2. Despite these 9 approved agents, outcomes for patients with r/r AML remain dismal and it remains an area of high medical need that could accommodate many new products with favorable safety and efficiency profiles.

We are pursuing CD33 because it is expressed in virtually all patients with AML. AML is known to be highly sensitive to radiation, which lends itself to our targeted radiotherapy approach. Also, AML has high cytogenetic and mutational heterogeneity, which targeted radiotherapy is agnostic to. Combination therapies are commonly used in hematologic indications, but we believe we are the only clinical stage Ac-225 based product candidate that is being explored in hematologic indications in combination with other modalities, including with the salvage chemotherapy regimen CLAG-M in fit patients with relapsed or refractory AML as well as in combination with the Bcl-2 inhibitor venetoclax in fit and unfit patients with relapsed or refractory AML.

In addition to developing targeted radiotherapies, we also own patents related to the manufacturing of Ac-225 in a cyclotron. Medical grade Ac-225 is largely supplied by the U.S. Department of Energy (“DOE”) derived from the natural decay of thorium-229 from so-called “thorium-cows”. Additional routes of Ac-225 production are being pursued by the DOE including the generation of new thorium cows and production via a cyclotron to increase supply. The DOE’s cyclotron production method for Ac-225 production leverages Actinium’s proprietary technology and know-how and presents an additional path towards production of high-quality Ac-225. Previously, we utilized our cyclotron production IP to create highly pure Ac-225. We are aware of at least six other government and non-government entities globally that have or expect to have ability to supply Ac-225 using various methods including ITM, Niowave, Terrapower, NorthStar Medical Radioisotopes, IONETIX Corporation, TRIUMF and Canadian Nuclear Laboratories that could be competitors should we elect to manufacture Ac-225 in the future. We believe our cyclotron method has the potential to produce robust amounts of highly pure Ac-225, which could address potential future Ac-225 supply constraints should multiple Ac-225 products gain regulatory approval.

Government Regulation

Governmental authorities in the United States and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing of radioimmunotherapy pharmaceutical products such as those being developed by us. In the United States, the FDA regulates such products under the Federal Food, Drug and Cosmetic Act (“FDCA”) and implements regulations. Failure to comply with applicable FDA requirements, both before and after approval, may subject us to administrative and judicial sanctions, such as a delay in approving or refusal by the FDA to approve pending applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

U.S. Food and Drug Administration Regulation

Our research, development and clinical programs, as well as our manufacturing and marketing operations, are subject to extensive regulation in the United States and other countries. Most notably, products that may in the future be sold in the United States are subject to regulation by the FDA. Certain of our product candidates in the United States will require FDA approval of a BLA prior to marketing. Foreign countries may require similar or more onerous approvals to manufacture or market these products.

FDA Approval Process for Biologics License Applications

Prior to testing a biological product on humans, the product must clear the preclinical testing stage. The goal of preclinical testing is to perform laboratory evaluations of the product's chemistry and formulation as well as evaluate the product's potential for adverse events by performing in vitro and animal studies. This information is packaged together and submitted to the FDA as part of an investigational new drug ("IND") application, which must be approved by the FDA before administering the product to human subjects in clinical trials.

From there, the product moves to the clinical stage, where it is administered to healthy volunteers or patients. The data gathered from the preclinical testing and clinical trials is used to support the BLA submission. The FDA must approve the BLA prior to commercial marketing of a biological product. The BLA must include information about product development, laboratory and animal studies, human trials, manufacturing information, the composition of the product, and proposed labeling. The approval process requires significant time and financial resources and does not guarantee that FDA will accept the BLA filing or ultimately approve the BLA.

The Prescription Drug User Fee Act, as amended ("PDUFA"), requires each BLA to be accompanied by a substantial user fee. The amount of the user fee changes on an annual basis. In addition to the BLA user fee, PDUFA also imposes an annual program fee for biological products. The FDA will waive or reduce the fee under limited circumstances, such as for first applications filed by small businesses.

Within 60 days following submission of the BLA, the FDA reviews the BLA submission for completion to determine if it will accept it for filing. The FDA may refuse to file the BLA if it deems the submission incomplete or not properly reviewable at the time of submission. For the BLA review process to proceed, the BLA must be resubmitted with the necessary additional information. After the BLA is accepted for filing, the FDA commences its substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, potent, and/or effective for its intended use, has an acceptable purity profile, and whether the product's manufacturing is consistent with current Good Manufacturing Processes ("cGMPs") to ensure that the product meets the appropriate standards for identity, safety, strength, quality, potency and purity.

The FDA may involve an advisory committee for novel biological products that present complex questions of safety or efficacy. The advisory committee typically consists of a panel that includes clinicians and other subject matter experts that assist with the reviewing and evaluating the product. While the advisory committee provides a recommendation for whether the product should be approved and under what conditions, the FDA is not bound to follow the recommendations. However, the advisory committee's recommendations are usually given significant consideration.

The FDA may also consider requiring a risk evaluation and mitigation strategy ("REMS") if it determines that one is necessary to ensure that the biological product is used safely. If the FDA requires a REMS, the BLA sponsor must develop and submit a proposed REMS for the BLA review process to move forward.

The manufacturer of the biological product is also subject to FDA inspection prior to the approval of the BLA. The purpose of the inspection is to determine whether the manufacturer adequately complies with the applicable cGMP requirements to ensure that the biological product is manufactured safely and within the required specifications. Additionally, the FDA may choose to inspect one or more clinical sites to assess compliance with IND trial requirements and good clinical practices ("GCPs"). Compliance with cGMP and GCP requirements involves significant expenditures of time, money, and effort for BLA sponsors due to associated training, recordkeeping, production, and quality control needs.

If the FDA decides not to approve the BLA in the form submitted, it will issue what is called a complete response letter that outlines the specific deficiencies it would like to see addressed. The deficiencies identified can be minor (e.g., labeling changes) or major (e.g., the need for additional clinical trials). The complete response letter may also include recommended actions the applicant may take to move closer towards securing an approval. At this point, applicants may choose to resubmit the BLA to address FDA's concerns or withdraw the application.

In addition, under the Pediatric Research Equity Act, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

Post-Approval Requirements

If the BLA is approved, the FDA may include additional conditions as part of its approval, such as limiting the approval by designating specific diseases for which the product may be used. Additionally, conditions may include requiring the labeling to include specific contraindications, warnings, or precautions, requiring post marketing clinical trials (sometimes referred to as Phase 4 clinical trials), and implementation of surveillance program to monitor the approved product once commercialized.

Products approved by the FDA under a BLA are subject to ongoing regulatory requirements, including, among other things, record-keeping requirements, adverse event reporting requirements, responsibility for reporting updated safety and efficacy information to FDA, sampling and distribution requirements, complying with advertising and promotion requirements, and complying with cGMPs.

Quality control and manufacturing procedures must continue to comply with cGMP requirements even after the BLA is approved. The cGMP regulations include, but are not limited to, requirements to ensure quality control, maintain appropriate manufacturing records and documentation, and the obligation to investigate and address deviations from cGMPs, when identified. Manufacturers are also required to register their establishments with the FDA and certain state agencies. The establishments are also subject to unannounced inspections by regulators.

The advertising and promotion of drug and biologic products are also subject to specific laws and regulations. These authorities provide standards for direct-to-consumer advertising, restrictions on promoting products for uses or to patient populations that are not described in the product's approved uses, known as "off-label" use, limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet.

Regulatory Enforcement

Failure to comply with applicable regulatory requirements can result in enforcement action by the FDA, the Nuclear Regulatory Commission or other regulatory authorities, which may result in sanctions, including but not limited to, untitled letters, warning letters, fines, injunctions, consent decrees and civil penalties; customer notifications or repair, replacement, refunds, recall, detention or seizure of our products; operating restrictions or partial suspension or total shutdown of production; refusing or delaying our requests for BLA premarket approval of new products or modified products; withdrawing BLA approvals that have already been granted; and refusal to grant export.

Additional Healthcare Laws

In addition to FDA regulations, several other types of state and federal laws may restrict our business activities, including certain healthcare laws. These laws include, without limitation, anti-kickback laws, false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item, good, facility or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other hand. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly and arrangements must meet every element to qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct *per se* illegal under the federal Anti-Kickback Statute. Instead, the arrangement will be evaluated on a case-by-case basis based on the facts and circumstances involved. Courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare program business, the federal Anti-Kickback Statute has been violated. Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the "Affordable Care Act," to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law that a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

Federal false claims laws, including the federal False Claims Act, and civil monetary penalties laws, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Whistleblower or qui tam provisions under the False Claims Act permit whistleblowers to sue in the name of the federal government for False Claims Act violations, and to share in the recovery from any award. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal civil and criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, if we engage in certain activities, we may be subject to data privacy and security regulation under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH. HIPAA imposes certain requirements on covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses, and their business associates and covered subcontractors that receive or obtain protected health information in connection with providing a service on behalf of a covered entity that involves the use or disclosure of individually identifiable health information.

Additionally, the federal Physician Payments Sunshine Act, created under the Affordable Care Act, and its implementing regulations, require certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually information related to certain payments or other transfers of value provided to physicians and any ownership and investment interests held by physicians or their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding payments and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

The majority of states also have statutes or regulations similar to the aforementioned federal healthcare laws, including fraud and abuse laws, some of which are broader in scope and apply to items and services reimbursed under Medicaid and other state programs, or, in some states, apply regardless of the payor. Many states also have some form of health information privacy or data security laws that could apply. Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments or other transfers of value provided to physicians and other healthcare providers and entities, marketing expenditures, or drug pricing. Certain state and local laws also require the registration of pharmaceutical sales representatives.

If our operations are found to be in violation of any of the healthcare regulatory laws described above or any other laws that apply to us, we may be subject to potentially significant criminal, civil and administrative penalties, damages, fines, disgorgement, imprisonment, additional reporting obligations and oversight (if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws), exclusion from participation in government healthcare programs, as well as contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Employees

As of March 25, 2022, we have 32 full-time employees including 20 with M.D., Ph.D. or other advanced degrees.

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunity for equity ownership, development programs that enable continued learning and growth, and an employment package that promotes wellness across all aspects of their lives, including healthcare, retirement planning, and paid time off. None of these employees are covered by a collective bargaining agreement, and we believe our relationship with our employees is good. We also engage consultants on an as-needed basis to supplement existing staff.

Recent Developments

Impact of COVID–19 Pandemic

The global health crisis caused by the novel coronavirus COVID-19 pandemic and its resurgences has and may continue to negatively impact global economic activity, which, despite progress in vaccination efforts, remains uncertain and cannot be predicted with confidence. In addition, the Omicron variant of COVID-19, which appears to be the most transmissible variant to date, has spread globally. The full impact of the Omicron variant, or any subsequent variant, cannot be predicted at this time, and could depend on numerous factors, including vaccination rates among the population, the effectiveness of COVID-19 vaccines against the Omicron variant and the response by governmental bodies and regulators. Given the ongoing and dynamic nature of the circumstances, it is difficult to predict the impact of the COVID-19 pandemic on our business.

Many countries around the world have continued to impose quarantines and restrictions on travel and mass gatherings to slow the spread of the virus. Accordingly, our ability to continue to operate our business may also be limited. Such events may result in a period of business, supply and drug product manufacturing disruption, and in reduced operations, any of which could materially affect our business, financial condition and results of operations. In response to COVID-19, we implemented remote working and thus far have not experienced a significant disruption or delay in our operations as it relates to the clinical development of our drug candidates. Such government-imposed precautionary measures may have been relaxed in certain countries or states, but there is no assurance that more strict measures will be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of the coronavirus, which may be more contagious and deadly than prior strains. Therefore, the COVID-19 pandemic may continue to affect our operation, may further divert the attention and efforts of the medical community to coping with COVID-19 and disrupt the marketplace in which we operate and may have a material adverse effect on our operations.

A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

We believe our earlier stage CD33 clinical trials will continue to recruit and enroll patients given the acute nature of relapsed or refractory AML. The continuation of the pandemic could adversely affect our planned clinical trial operations, including our ability to conduct the trials on the expected timelines and recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if their geography is impacted by the pandemic. Further, the continuation and/or resurgence of the COVID-19 pandemic could result in delays in our clinical trials due to prioritization of hospital resources toward the pandemic, restrictions in travel, potential unwillingness of patients to enroll in trials at this time, or the inability of patients to comply with clinical trial protocols if quarantines or travel restrictions impede patient movement or interrupt healthcare services. In addition, we rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, and the pandemic may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us, which may result in delays or hinder our ability to collect data from our clinical trials.

Additionally, COVID-19 may result in delays in receiving approvals from local and foreign regulatory authorities, delays in necessary interactions with IRB's or Institutional Review Boards, local and foreign regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees.

To date, COVID-19 has not had a financial impact on our company. We continue to monitor the impacts of COVID-19 on the global economy and on our business operations. Although we expect that vaccinations for COVID-19 will continue to improve conditions, the ultimate impact from COVID-19 on our business operations and financial results during 2022 will depend on, among other things, the ultimate severity and scope of the pandemic, including the new variants of the virus, the pace at which governmental and private travel restrictions and public concerns about public gatherings will ease, the rate at which historically large increases in unemployment rates will decrease, if at all, and whether, and the speed with which the economy recovers. We are not able to fully quantify the impact that these factors will have on our financial results during 2022 and beyond.

ITEM 1A. RISK FACTORS

In analyzing our company, you should consider carefully the following risk factors, together with all of the other information included in this Annual Report on Form 10-K. Factors that could cause or contribute to differences in our actual results include those discussed in the following subsection, as well as those discussed above in "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this Annual Report on Form 10-K. Each of the following risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our company. The risks and uncertainties described below are not the only ones we face. Additional risks not currently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Summary of Risk Factors

We are providing the following summary of the risk factors contained in this Annual Report on Form 10-K to enhance the readability and accessibility of our risk factor disclosures. We encourage you to carefully review the full risk factors contained in this Annual Report on Form 10-K in their entirety for additional information regarding the material factors that make an investment in our securities speculative or risky. These risks and uncertainties include, but are not limited to, the following:

- We are a clinical-stage company and have generated no revenue from commercial sales to date;
- We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses in the future;
- If we fail to obtain additional financing, we will be unable to continue or complete our product development and you will likely lose your entire investment;
- We are highly dependent on the success of Iomab-B and the SIERRA trial and we may not be able to complete the necessary clinical development or our development efforts may not result in the data necessary to receive regulatory approval;
- Our business could be adversely affected by the effects of health epidemics, including the global COVID-19 pandemic;
- We have not demonstrated that any of our products are safe and effective for any indication and will continue to expend substantial time and resources on clinical development before any of our current or future product candidates will be eligible for FDA approval, if ever;
- Our clinical trials may fail to demonstrate adequately the efficacy and safety of our product candidates, which would prevent or delay regulatory approval and commercialization;
- Preliminary, Interim, and "top-line" data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.;
- Healthcare legislative reform measures intended to increase pressure to reduce prices of pharmaceutical products paid for by Medicare or, otherwise, affect the federal regulation of the U.S. healthcare system could have a material adverse effect our business, future revenue, if any, and results of operations;
- We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates;
- We currently depend on a single third-party manufacturer to produce our pre-clinical and clinical trial drug supplies. Any disruption in the operations of our current third-party manufacturer, or other third-party manufacturers we may engage in the future, could adversely affect our business and results of operations;

- Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences;

- Our patent position is highly uncertain and involves complex legal and factual questions.

- The use of hazardous materials, including radioactive and biological materials, in our research and development efforts imposes certain compliance costs on us and may subject us to liability for claims arising from the use or misuse of these materials;

- We are highly dependent on our key personnel, and the demand for talent in the biotechnology industry is highly competitive; if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement or execute our business strategy;

- Certain provisions of our Certificate of Incorporation and Bylaws and Delaware law make it more difficult for a third party to acquire us and make a takeover more difficult to complete, even if such a transaction were in our stockholders' interest; and

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

Risks Related to Our Business

We are a clinical-stage company and have generated no revenue from commercial sales to date.

We are a clinical-stage biopharmaceutical company with a limited operating history. We have no products approved for commercial sale and have not generated any revenue from product sales to date. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses in the future.

We are not profitable and have incurred losses in each period since our inception. As of December 31, 2021 and December 31, 2020, we had an accumulated deficit of $255.7 million and $231.0 million, respectively. We reported a net loss of $24.8 million and $22.2 million for the years ended December 31, 2021 and 2020, respectively. We expect to continue to operate at a net loss as we continue our research and development efforts, continue to conduct clinical trials and develop manufacturing, sales, marketing and distribution capabilities. There can be no assurance that the products under development by us will be approved for sale in the United States or elsewhere. Furthermore, there can be no assurance that if such products are approved, they will be successfully commercialized, which would have an adverse effect on our business prospects, financial condition and results of operation.

If we fail to obtain additional financing, we will be unable to continue or complete our product development and you will likely lose your entire investment.

In August 2020, we entered into the Capital on Demand™ Sales Agreement with JonesTrading, pursuant to which we may sell, from time to time, through or to JonesTrading, up to an aggregate of $200 million of our common stock. Shares of common stock are offered pursuant to our shelf registration statement filed with the SEC on August 7, 2020. For the year ended December 31, 2021, we sold 4.6 million shares of common stock, resulting in net proceeds of $35.3 million. As of the date of filing this report, we expect that our existing resources will be more than sufficient to fund our planned operations for more than 12 months following the date of this report.

Our business or operations may change in a manner that would consume available funds more rapidly than anticipated and substantial additional funding may be required to maintain operations, fund expansion, develop new or enhanced products, acquire complementary products, business or technologies or otherwise respond to competitive pressures and opportunities, such as a change in the regulatory environment or a change in preferred cancer treatment modalities. However, we may not be able to secure funding when we need it or on favorable terms or indeed on any terms. In addition, from time to time, we may not be able to secure enough capital in a timely enough manner which may cause the generation of a going-concern opinion from our auditors which can and may impair our stock market valuation and also our ability to finance on favorable terms or indeed on any terms.

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders.

If we cannot raise adequate funds to satisfy our capital requirements, we will have to delay, scale back or eliminate our research and development activities, clinical studies or future operations. We may also be required to obtain funds through arrangements with collaborators, which arrangements may require us to relinquish rights to certain technologies or products that we otherwise would not consider relinquishing, including rights to future product candidates or certain major geographic markets. We may further have to license our technology to others. This could result in sharing revenues which we might otherwise have retained for ourselves. Any of these actions may harm our business, financial condition and results of operations.

The amount of funding we will need depends on many factors, including the progress, timing and scope of our product development programs; the progress, timing and scope of our preclinical studies and clinical trials; the time and cost necessary to obtain regulatory approvals; the time and cost necessary to further develop manufacturing processes and arrange for contract manufacturing; our ability to enter into and maintain collaborative, licensing and other commercial relationships; and our partners' commitment of time and resources to the development and commercialization of our products.

We have limited access to the capital markets and even if we can raise additional funding, we may be required to do so on terms that are dilutive to you.

We have limited access to the capital markets to raise funds. The capital markets have been unpredictable in the recent past for radioisotope and other oncology companies and unprofitable companies such as ours. In addition, it is generally difficult for development-stage companies to raise capital under current market conditions. The amount of capital that a company such as ours is able to raise often depends on variables that are beyond our control. As a result, we may not be able to secure financing on terms attractive to us, or at all. If we are able to consummate a financing arrangement, the amount raised may not be sufficient to meet our future needs. If adequate funds are not available on acceptable terms, or at all, our business, including our technology licenses, results of operations, financial condition and our continued viability will be materially adversely affected.

We are highly dependent on the success of Iomab-B and the SIERRA trial and we may not be able to complete the necessary clinical development or our development efforts may not result in the data necessary to receive regulatory approval.

We have completed patient enrollment in the pivotal Phase 3 SIERRA trial (Study of Iomab-B in Elderly Relapsed or Refractory AML), a 150-patient multi-center randomized trial that will compare outcomes of patients who receive Iomab-B and a BMT to those patients receiving physician's choice of salvage chemotherapy, defined as conventional care, as no standard of care exists for this patient population. The SIERRA trial may be unsuccessful and fail to demonstrate a safety and efficacy profile that is necessary to receive favorable regulatory approval. Even if Iomab-B receives favorable regulatory approval, we may not be successful in securing adequate reimbursement or establishing successful commercial operations. Any or all of these factors could have a material adverse impact on our business and ability to continue operations.

We may be unable to establish sales, marketing and commercial supply capabilities.

We do not currently have, nor have we ever had, commercial sales and marketing capabilities. If any of our product candidates become approved, we would have to build and establish these capabilities in order to commercialize our approved product candidates. The process of establishing commercial capabilities will be expensive and time consuming. Even if we are successful in building sales and marketing capabilities, we may not be successful in commercializing any of our product candidates. Any delays in commercialization or failure to successfully commercialize any product candidate may have material adverse impacts on our business and ability to continue operations.

Our business could be adversely affected by the effects of health epidemics, including the global COVID-19 pandemic.

The global health crisis caused by the novel coronavirus COVID-19 pandemic and its resurgences has and may continue to negatively impact global economic activity, which, despite progress in vaccination efforts, remains uncertain and cannot be predicted with confidence. In addition, the Omicron variant of COVID-19, which appears to be the most transmissible variant to date, has spread globally. The full impact of the Omicron variant, or any subsequent variant, cannot be predicted at this time, and could depend on numerous factors, including vaccination rates among the population, the effectiveness of COVID-19 vaccines against the Omicron variant and the response by governmental bodies and regulators. Given the ongoing and dynamic nature of the circumstances, it is difficult to predict the impact of the COVID-19 pandemic on our business.

Many countries around the world have continued to impose quarantines and restrictions on travel and mass gatherings to slow the spread of the virus. Accordingly, our ability to continue to operate our business may also be limited. Such events may result in a period of business, supply and drug product manufacturing disruption, and in reduced operations, any of which could materially affect our business, financial condition and results of operations. In response to COVID-19, we implemented remote working and thus far have not experienced a significant disruption or delay in our operations as it relates to the clinical development of our drug candidates. Such government-imposed precautionary measures may have been relaxed in certain countries or states, but there is no assurance that more strict measures will be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of the coronavirus, which may be more contagious and deadly than prior strains. Therefore, the COVID-19 pandemic may continue to affect our operation, may further divert the attention and efforts of the medical community to coping with COVID-19 and disrupt the marketplace in which we operate and may have a material adverse effect on our operations.

A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

We believe our earlier stage CD33 clinical trials will continue to recruit and enroll patients given the acute nature of relapsed or refractory AML. The continuation of the pandemic could adversely affect our planned clinical trial operations, including our ability to conduct the trials on the expected timelines and recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if their geography is impacted by the pandemic. Further, the continuation and/or resurgence of the COVID-19 pandemic could result in delays in our clinical trials due to prioritization of hospital resources toward the pandemic, restrictions in travel, potential unwillingness of patients to enroll in trials at this time, or the inability of patients to comply with clinical trial protocols if quarantines or travel restrictions impede patient movement or interrupt healthcare services. In addition, we rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, and the pandemic may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us, which may result in delays or hinder our ability to collect data from our clinical trials.

Additionally, COVID-19 may result in delays in receiving approvals from domestic and foreign regulatory authorities, delays in necessary interactions with Institutional Review Boards ("IRBs"), domestic and foreign regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees.

We continue to monitor the impacts of COVID-19 on the global economy and on our business operations. However, the ultimate impact from COVID-19 on our business operations and financial results during 2022 will depend on, among other things, the ultimate severity and scope of the pandemic, including the new variants of the virus, the pace at which governmental and private travel restrictions and public concerns about public gatherings will ease, the rate at which historically large increases in unemployment rates will decrease, if at all, and whether, and the speed with which the economy recovers. We are not able to fully quantify the impact that these factors will have on our financial results during 2022 and beyond.

Our business is subject to cybersecurity risks.

Our operations are increasingly dependent on information technologies and services. Threats to information technology systems associated with cybersecurity risks and cyber incidents or attacks continue to grow, and include, among other things, storms and natural disasters, terrorist attacks, utility outages, theft, viruses, phishing, malware, design defects, human error, and complications encountered as existing systems are maintained, repaired, replaced, or upgraded. Risks associated with these threats include, among other things:

- theft or misappropriation of funds;
- loss, corruption, or misappropriation of intellectual property, or other proprietary, confidential or personally identifiable information (including supplier, clinical data or employee data);
- disruption or impairment of our and our business operations and safety procedures;
- damage to our reputation with our potential partners, patients and the market;
- exposure to litigation;
- increased costs to prevent, respond to or mitigate cybersecurity events.

Although we utilize various procedures and controls to mitigate our exposure to such risk, cybersecurity attacks and other cyber events are evolving and unpredictable. Moreover, we have no control over the information technology systems of third parties conducting our clinical trials, our suppliers, and others with which our systems may connect and communicate. As a result, the occurrence of a cyber incident could go unnoticed for a period time.

We have cybersecurity insurance coverage in the event we become subject to various cybersecurity attacks, however, we cannot ensure that it will be sufficient to cover any particular losses we may experience as a result of such cyberattacks. Any cyber incident could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Regulation

The FDA or comparable foreign regulatory authorities may disagree with our regulatory plans and we may fail to obtain regulatory approval of our product candidates.

Our products are subject to rigorous regulation by the FDA and numerous other federal, state and foreign governmental authorities. The process of seeking regulatory approval to market an antibody radiation-conjugate product is expensive and time-consuming, and, notwithstanding the effort and expense incurred, approval is never guaranteed. If we are not successful in obtaining timely approval of our products from the FDA, we may never be able to generate significant revenue and may be forced to cease operations. In particular, the FDA permits commercial distribution of a new antibody radiation-conjugate product only after a BLA for the product has received FDA approval. The BLA process is costly, lengthy and inherently uncertain. Any BLA filed by us will have to be supported by extensive data, including, but not limited to, technical, preclinical, clinical trial, chemistry, manufacturing and controls ("CMC") and labeling data, to demonstrate to the FDA's satisfaction the safety and efficacy of the product for its intended use. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

The approval process in the United States and in other countries could result in unexpected and significant costs for us and consume management's time and other resources. The FDA and other foreign regulatory agencies could ask us to supplement our submissions, collect non-clinical data, conduct additional clinical trials or engage in other time-consuming actions, or it could simply deny our applications. In addition, even if we obtain approval to market our products in the United States or in other countries, the approval could be revoked, or other restrictions imposed if post-market data demonstrates safety issues or lack of effectiveness. We cannot predict with certainty how, or when, the FDA or other regulatory authorities will act. If we are unable to obtain the necessary regulatory approvals, our financial condition and cash flow may be materially adversely affected, and our ability to grow domestically and internationally may be limited. Additionally, even if we obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications that we request. The Company's products may not be approved for the specific indications that are most necessary or desirable for successful commercialization or profitability.

We have not demonstrated that any of our products are safe and effective for any indication and will continue to expend substantial time and resources on clinical development before any of our current or future product candidates will be eligible for FDA approval, if ever.

We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to development of our existing and contemplated biological product candidates. Accordingly, our business currently depends heavily on the successful development, FDA approval, and commercialization of such candidates, which may never receive FDA approval or be successfully commercialized even if FDA approval is received. The research, testing, manufacturing, labeling, approval, sale, marketing, and distribution of our biological product candidates are, and will remain, subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, as applicable. We are currently not permitted to market any of our current or future product candidates in the United States until we receive FDA approval (of each) via the BLA process. To date, we have two product candidates in clinical development and have not-yet submitted a BLA for any of our candidates and, for many such candidates, do not expect to be in a position to do so for the foreseeable future, as there are numerous developmental steps that must be completed before we can prepare and submit a BLA.

In the United States, the FDA regulates pharmaceutical and biological product candidates under the FDCA and the Public Health Service Act ("PHSA"), as well as their respective implementing regulations. Such products and product candidates are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations requires the expenditure of substantial time and financial resources. The process required by the FDA before a drug or biological product may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies in accordance with FDA's good laboratory practices ("GLPs") and applicable requirements for the humane use of laboratory animals or other applicable regulations;

- submission to the FDA of an Investigational New Drug ("IND"), which must become effective before human clinical trials in the United States may begin;

- performance of adequate and well-controlled human clinical trials in accordance with FDA's IND regulations, GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;

- submission to the FDA of a BLA for marketing approval that meets applicable requirements to ensure the continued safety, purity, and potency of the product that is the subject of the BLA based on results of preclinical testing and clinical trials;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced, to assess compliance with cGMPs and assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;

- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA; and

- FDA review and approval, or denial, of the BLA.

Before testing any biological product candidate in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs. The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin or that, for those that have already commenced under an active IND, that issues will not arise that suspend or terminate such trials.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations composing the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in subjects.

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

- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk to benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

After the completion of clinical trials of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. The FDA may grant deferrals for submission of data, or full or partial waivers. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all. Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. Our product candidates are in the earliest stages of clinical development and, therefore, a long way from BLA submission. We cannot predict with any certainty if or when we might submit a BLA for regulatory approval for our product candidates or whether any such BLA will be approved by the FDA. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. For example, the FDA may not agree with our proposed endpoints for any clinical trial we propose, which may delay the commencement of our clinical trials. The clinical trial process is also lengthy and requires substantial time and effort.

In December 2015, the FDA cleared our IND filing for Iomab-B and we have completed patient enrollment of a randomized, controlled, pivotal Phase 3 clinical trial under such IND to study Iomab-B in patients 55 years of age or older with relapsed or refractory AML. Assuming the Phase 3 trial meets its endpoints and there are no unexpected issues or delays, it is expected to form the basis for a BLA for Iomab-B for use in preparing and conditioning AML patients for a BMT. Additionally, there are physician IND trials at the FHCRC that have been conducted or are currently ongoing at FHCRC with Iomab-B (for other target indications) and the apamistamab antibody (formerly known as BC8) we licensed. And, we have multiple Phase 1 and Phase 2 clinical trials ongoing and others that we have planned but not-yet commenced, for our other drug candidates under our own sponsorship and multiple investigator-initiated trials ongoing. Except for Iomab-B (for patients with AML), we expect that the clinical trials we need to conduct to be in a position to submit BLAs for our product candidates currently in-development will take, at least, several years to complete. Moreover, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. Also, the results of early preclinical and clinical testing may not be predictive of the results of subsequent clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies. And, preclinical and clinical data are often susceptible to multiple interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have, nonetheless, failed to obtain marketing approval of their products. Success in preclinical testing and early clinical trials does not ensure that later clinical trials, which involve many more subjects, and the results of later clinical trials may not replicate the results of prior clinical trials and preclinical testing. Any failure or substantial delay in our product development plans may have a material adverse effect on our business.

We may encounter substantial delays in our clinical trials or may not be able to conduct our trials on the timelines we expect.

We cannot predict whether we will encounter problems with any of our ongoing or planned clinical trials that will cause us or regulatory authorities to delay, suspend, or discontinue clinical trials or to delay the analysis of data from ongoing clinical trials. Any of the following could delay or disrupt the clinical development of our product candidates and potentially cause our product candidates to fail to receive regulatory approval:

- conditions imposed on us by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in receiving, or the inability to obtain, required approvals from IRBs or other reviewing entities at clinical sites selected for participation in our clinical trials;
- delays in enrolling patients into clinical trials;
- a lower than anticipated retention rate of patients in clinical trials;
- the need to repeat or discontinue clinical trials as a result of inconclusive or negative results or unforeseen complications in testing or because the results of later trials may not confirm positive results from earlier preclinical studies or clinical trials;
- inadequate supply, delays in distribution, deficient quality of, or inability to purchase or manufacture drug product, comparator drugs or other materials necessary to conduct our clinical trials;
- unfavorable FDA or other foreign regulatory inspection and review of a clinical trial site or records of any clinical or preclinical investigation;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials, which may occur even if they were not observed in earlier trials or only observed in a limited number of participants;
- a finding that the trial participants are being exposed to unacceptable health risks;
- the placement by the FDA or a foreign regulatory authority of a clinical hold on a trial; or
- delays in obtaining regulatory agency authorization for the conduct of our clinical trials.

We may suspend, or the FDA or other applicable regulatory authorities may require us to suspend, clinical trials of a product candidate at any time if we or they believe the patients participating in such clinical trials, or in independent third-party clinical trials for drugs based on similar technologies, are being exposed to unacceptable health risks including but not limited to unacceptable or suboptimal factors related to toxicity, clinical efficacy, imbalances in safety and efficacy profiles or for other reasons.

Further, individuals involved with our clinical trials may serve as consultants to us from time to time and receive stock options or cash compensation in connection with such services. If these relationships and any related compensation to the clinical investigator carrying out the study result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized. The delay, suspension or discontinuation of any of our clinical trials, or a delay in the analysis of clinical data for our product candidates, for any of the foregoing reasons, could adversely affect our efforts to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our financial results.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a trial, or a data safety monitoring board, or DSMB (Data Safety Monitoring Board)/DMC (Data Monitoring Committee), overseeing the clinical trial at issue, or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- varying interpretation of data by the FDA or similar foreign regulatory authorities;
- failure to achieve primary or secondary endpoints or other failure to demonstrate efficacy;
- unforeseen safety issues; or
- lack of adequate funding to continue the clinical trial.

Modifications to our product candidates may require federal approvals.

The BLA application is the vehicle through which the company may formally propose that the FDA approve a new pharmaceutical for sale and marketing in the United States. Once a particular product candidate receives FDA approval, expanded uses or uses in new indications of our products may require additional human clinical trials and new regulatory approvals, including additional IND and BLA submissions and premarket approvals before we can begin clinical development, and/or prior to marketing and sales. If the FDA requires new approvals for a particular use or indication, we may be required to conduct additional clinical studies, which would require additional expenditures and harm our operating results. If the products are already being used for these new indications, we may also be subject to significant enforcement actions.

Conducting clinical trials and obtaining approvals is a time-consuming process, and delays in obtaining required future approvals could adversely affect our ability to introduce new or enhanced products in a timely manner, which in turn would have an adverse effect on our business prospects, financial condition and results of operation.

The FDA or comparable foreign regulatory authorities may disagree with our regulatory plans, and we may fail to obtain regulatory approval of our product candidates.

In June 2012, we acquired rights to apamistamab, a clinical stage anti-CD45 monoclonal antibody with safety and efficacy data in more than 300 patients in need of a BMT. Iomab-B is our product candidate that links I-131 to apamistamab that is being studied in the pivotal Phase 3 SIERRA trial. Product candidates utilizing apamistamab would require BLA approval before they can be marketed in the United States. We are also evaluating Iomab-ACT, which uses a lower dose I-131 for lymphodepletion prior to CAR-T or adoptive cell therapy. We are currently evaluating clinical trials that would use our construct for lymphodepletion. Our lintuzumab-Ac-225 product candidate is also being studied in several Phase 1 trials under our sponsorship and investigator-initiated trials in patients with r/r AML. Product candidates utilizing the lintuzumab antibody would require BLA approval before they can be marketed in the United States. We are in the early stages of evaluating other product candidates consisting of conjugates of Ac-225 with human or humanized antibodies for pre-clinical and clinical development in other types of cancer. The FDA may not approve these products for the indications that are necessary or desirable for successful commercialization. The FDA may fail to approve any BLA we submit for new product candidates or for new intended uses or indications for approved products or future product candidates. Failure to obtain FDA approval for our products in the proposed indications would have a material adverse effect on our business prospects, financial condition and results of operations.

Clinical trials necessary to support approval of our product candidates are time-consuming and expensive.

Initiating and completing clinical trials necessary to support FDA approval of a BLA for Iomab-B, CD33 program candidates, and other product candidates, is a time-consuming and expensive process, and the outcome is inherently uncertain. Moreover, the results of early clinical trials are not necessarily predictive of future results, and any product candidate we advance into clinical trials may not have favorable results in later clinical trials. We worked with the FDA to develop the SIERRA clinical trial to test the safety and efficacy of Iomab-B in patients with relapsed or refractory AML who are age 55 and above prior to a BMT. This trial is designed to support a BLA filing for marketing approval by the FDA, pending results from the trial. In addition to clinical data, a BLA filing encompasses preclinical, CMC, labeling and other information. Even if the clinical data from the SIERRA trial is positive, there can be no assurances that the BLA filing we produce will meet all of the FDA's requirements or that they will not request additional information or studies, which may delay the FDA's review or we may not be able to produce. We have also worked with the FDA to develop a regulatory pathway for lintuzumab-Ac-225 in patients with high-risk MDS that consists of a dose-confirming Phase 1 trial that can be followed by a randomized, controlled pivotal trial that could support a BLA filing. To date, we have not initiated this clinical trial and we may never elect or be able to do so. There can be no assurance that the data generated during the trial will meet our chosen safety and effectiveness endpoints or otherwise produce results that will eventually support the filing or approval of a BLA. Even if the data from this trial are favorable, the data may not be predictive of the results of any future clinical trials.

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

From time to time, we may publicly disclose preliminary, interim, and top-line data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change as more patient data become available or following a more comprehensive review of the data related to the particular study or trial. For example, at the ASH annual meeting in December 2021, we presented safety and feasibility data available at the time of data submission from 100% patient enrollment from the SIERRA trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. Our clinical trials may be open label studies and certain of our clinical development and or operations staff may review interim or preliminary safety or efficacy data during routine data collection, cleaning and analysis from time to time. Interim or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. Preliminary, interim or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line, interim or preliminary data we previously published. As a result, top-line, interim and preliminary data should be viewed with caution until the final data are available.

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

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, top-line or preliminary data that we report differ from final results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Our clinical trials may fail to demonstrate adequately the efficacy and safety of our product candidates, which would prevent or delay regulatory approval and commercialization.

Even if our clinical trials are completed as planned, we cannot be certain that their results will support our product candidate claims or that the FDA or foreign authorities will agree with our conclusions regarding them. Success in pre-clinical studies and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the later trials will replicate the results of prior trials and pre-clinical studies. The clinical trial process may fail to demonstrate that our product candidates are safe and effective for the proposed indicated uses. If FDA concludes that the clinical trials for Iomab-B, Actimab-A, or any other product candidate for which we might seek approval, have failed to demonstrate safety and effectiveness, we would not receive FDA approval to market that product candidate in the United States for the indications sought. In addition, such an outcome could cause us to abandon the product candidate and might delay development of others. Any delay or termination of our clinical trials will delay or preclude the filing of any submissions with the FDA and, ultimately, our ability to commercialize our product candidates and generate revenues. It is also possible that patients enrolled in clinical trials will experience adverse side effects that are not currently part of a product candidate's profile.

The intellectual property related to antibodies we have licensed has expired or likely expired.

The key patents related to the humanized antibody, lintuzumab, which we use in our CD33 program product candidates have expired. It is generally possible that others may be eventually able to use an antibody with the same sequence, and we will then need to rely on additional patent protection covering alpha particle drug products comprising Ac-225. Our final drug construct consists of the lintuzumab antibody labeled with the isotope Ac-225. We have licensed issued patents that relate to the linker technology we use to conjugate the isotope to the antibody. Further, we own issued and pending patents related to methods for drug conjugation and isotope labeling and for methods of isotope production. In addition, we possess trade secrets and know how related to the manufacturing and use of isotopes. Any competing product based on the lintuzumab antibody is likely to require several years of development before achieving our product candidate's current status and may be subject to significant regulatory hurdles but such development by others is nevertheless a possibility that could negatively impact our business in the future. We own 2 issued U.S. patents, 1 issued European patent (validated as a national patent in several countries) and 1 issued Japanese patent that relate to the composition of our Iomab-B product candidate. Several patent applications relating to Iomab-B are also pending in the U.S. and internationally. We have and may continue to file patents related to Iomab-B that can provide barriers to entry but there is no certainty that these patents will be granted or such granting thereof will adequately prevent others from seeking to replicate and use the apamistamab antibody or the construct. We have pending patents related to radioimmunoconjugate composition, formulation administration, and methods of use in solid or liquid cancers. This matter includes composition, administration, and methods of treatment for our products Actimab-A and Iomab-B. Any competing product based on the antibody used in Iomab-B is likely to require several years of development before achieving our product candidate's current status and may be subject to significant regulatory hurdles but such development by others is nevertheless a possibility that could negatively impact our business in the future.

Our CD33 program clinical trials are testing the same drug construct.

Our CD33 program is comprised of several clinical trials including investigator-initiated trials in AML that are studying the same drug construct consisting of lintuzumab-Ac-225. Negative results from any of these trials could negatively impact our ability to enroll or complete our other trials studying lintzumab-Ac-225. Additionally, negative outcomes including safety concerns, may result in the FDA discontinuing other trials utilizing lintuzumab-Ac-225.

We may be unable to obtain a sufficient supply of isotopes to support clinical development or at commercial scale.

Iodine-131 is a key component of our Iomab-B drug candidate. We currently source medical grade I-131 from three suppliers including two leading global manufacturers. Currently, there is sufficient supply of I-131 to advance our ongoing SIERRA clinical trial, support additional trials we may undertake utilizing I-131 and for commercialization of Iomab-B. We continually evaluate I-131 manufacturers and suppliers and intend to have multiple qualified suppliers prior to the commercial launch of Iomab-B. While we consider I-131 to be commoditized and obtainable through several suppliers, there can be no guarantee that we will be able to secure I-131 or obtain I-131 on terms that are acceptable to us.

Actinium-225 is a key component of our CD33 ARC program, AWE platform and other drug candidates that we might consider for development with the Ac-225 payload. There are adequate quantities of Ac-225 available today to meet our current needs via our present supplier, the Department of Energy (“DOE”). The current Ac-225 currently supplied to Actinium’s clinical trials from the DOE is derived from the natural decay of thorium-229 from so-called ‘thorium-cows’ and is able to produce sufficient quantities that are several multiples of the amount of Ac-225 we require to supply our clinical programs through to early commercialization phase. The DOE is also producing Ac-225 from a recently developed alternative route for Ac-225 production via a linear accelerator that is currently being evaluated by Actinium. Initial preclinical and modelling results have indicated that the linear accelerator sourced Ac-225 does not impact labelling efficiency and expected distribution. In accordance with representations made by the DOE, the capacity of Ac-225 from this route is expected to be sufficient to supply all of Actinium’s pipeline and commercial Ac-225 needs and support new program expansion by not just Actinium but also other companies that are developing Ac-225 based products. Additional routes of Ac-225 production are being pursued by the DOE including the generation of new thorium cows and production via a cyclotron. The cyclotron production method for Ac-225 production leverages Actinium’s proprietary technology and know-how and presents an additional path towards production of high-quality Ac-225 that would be able to satisfy commercial needs. In addition, we are aware of at least six other government and non-government entities globally including the U.S., Canada, Russia, Belgium, France and Japan that have, or expect to have ability to supply Ac-225 or equipment for its production within the timeframes relevant to the potential first commercial approval of our Ac-225 ARC.

Our contract for supply of this isotope from the DOE must be renewed yearly, we recently renewed our contract to extend through the end of 2022. While we expect this contract will continue to be renewed at the end of its term as it has since 2009, there can be no assurance that the DOE will renew the contract or that change its policies that allow for the sale of isotope to us. Failure to acquire sufficient quantities of medical grade Ac-225 would make it impossible to effectively complete clinical trials and to commercialize any Ac-225 based drug candidates that we may develop and would materially harm our business.

Our ability to conduct clinical trials to advance our ARC drug candidates is dependent on our ability to obtain the radioisotopes I-131, Ac-225 and other isotopes we may choose to utilize in the future. Currently, we are dependent on third party manufacturers and suppliers for our isotopes. These suppliers may not perform their contracted services or may breach or terminate their agreements with us. Our suppliers are subject to regulations and standards that are overseen by regulatory and government agencies and we have no control over our suppliers’ compliance to these standards. Failure to comply with regulations and standards may result in their inability to supply isotope could result in delays in our clinical trials, which could have a negative impact on our business. We have developed intellectual property, know-how and trade secrets related to the manufacturing process of Ac-225. While we have manufactured medical grade Ac-225 of a purity compared to the cyclotron sourced material in the past, this activity was terminated due to operating cost reasons and we currently do not have experience in manufacturing medical grade Ac-225 and may not obtain the resources necessary to establish our own manufacturing capabilities in future. Our inability to build out and establish our own manufacturing facilities would require us to continue to rely on third party suppliers as we currently do. However, based on our current third-party suppliers and potential future suppliers of Ac-225 we expect to have adequate isotope supply to support our current ongoing clinical trials, current AWE program activities and commercialization should our drug candidates receive approval.

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

The timely completion of clinical trials in accordance with their protocols depends on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol;
- the size of the study population required for analysis of the trial’s primary endpoints;

- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and expertise;
- competing clinical trials for similar or alternate therapeutic treatments;
- clinician's and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete a clinical trial.

In addition, refractory patients, which several of our trials are enrolling, participating in clinical trials are seriously and often terminally ill and therefore may not complete the clinical trial due to reasons including comorbid conditions or occurrence of adverse medical events related or unrelated to the investigational products, or death. Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment will result in increased costs or affect the timing of our planned trials, which could adversely affect our ability to advance the development of our product candidates.

FDA may take actions that would prolong, delay, suspend, or terminate clinical trials of our product candidates, which may delay or prevent us from commercializing our product candidates on a timely basis.

There can be no assurance that the data generated in our clinical trials will be acceptable to FDA or that if future modifications during the trial are necessary, that any such modifications will be acceptable to FDA. Certain modifications to a clinical trial protocol made during the course of the clinical trial have to be submitted to the FDA. This could result in the delay or halt of a clinical trial while the modification is evaluated. In addition, depending on the quantity and nature of the changes made, FDA could take the position that some or all of the data generated by the clinical trial is not usable because the same protocol was not used throughout the trial. This might require the enrollment of additional subjects, which could result in the extension of the clinical trial and the FDA delaying approval of a product candidate. If the FDA believes that its prior approval is required for a particular modification, it can delay or halt a clinical trial while it evaluates additional information regarding the change.

Any delay or termination of our current or future clinical trials as a result of the risks summarized above, including delays in obtaining or maintaining required approvals from IRBs, delays in patient enrollment, the failure of patients to continue to participate in a clinical trial, and delays or termination of clinical trials as a result of protocol modifications or adverse events during the trials, may cause an increase in costs and delays in the filing of any submissions with the FDA, delay the approval and commercialization of our product candidates or result in the failure of the clinical trial, which could adversely affect our business, operating results and prospects. Lengthy delays in the completion of our Iomab-B clinical trials would adversely affect our business and prospects and could cause us to cease operations.

We have obtained orphan drug designation from FDA for two of our current product candidates and intend to pursue such designation for other candidates and indications in the future, but we may be unable to obtain such designations or to maintain the benefits associated with any orphan drug designations we have received or may receive in the future.

We have received orphan drug designation for Iomab-B and lintuzumab-CD33 ARC for treatment of AML in both the United States and the EU. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making available a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Similarly, the EMA grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU.

Orphan drug designation neither shortens the development time or regulatory review time of a drug or biologic nor gives the drug or biologic any advantage in the regulatory review or approval process. In the United States, orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages, and application fee waivers. In addition, if a product candidate receives the first FDA approval for the indication for which it has orphan designation, such product is entitled, upon approval, to seven years of orphan-drug exclusivity, during which the FDA may not approve any other application to market the same drug for the same indication, unless a subsequently approved product is clinically superior to orphan drug or where the manufacturer is unable to assure sufficient product quantity in the applicable patient population. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Even if we obtain (or have obtained) orphan drug designation for certain product candidates, we may not be the first to obtain marketing approval for such candidates for the applicable indications due to the uncertainties inherent in the development of novel biologic products. And, an orphan drug candidate may not receive orphan-drug exclusivity upon approval if such candidate is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Finally, even if we successfully obtain orphan-drug exclusivity for an orphan drug candidate upon approval, such exclusivity may not effectively protect the product from competition because (i) different drugs with different active moieties can be approved for the same condition; and (ii) the FDA or EMA can also subsequently approve a subsequent product with the same active moiety and for the same indication as the orphan drug if the later-approved drug if deemed clinically superior to the orphan drug.

Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review.

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. In addition, the FDA could require us to conduct another study to obtain additional safety or biomarker information. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party suppliers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;

- fines, warning letters or holds on clinical trials;

- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;

- product seizure or detention, or refusal to permit the import or export of our product candidates; and

- injunctions or the imposition of civil or criminal penalties.

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

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates which could limit our sales of our product candidates, if approved.

The commercial success of our product candidates in both domestic and international markets will be substantially dependent on whether third-party coverage and reimbursement is available for patients that use our products. However, the availability of insurance coverage and reimbursement for newly approved cancer therapies is uncertain, and therefore, third-party coverage may be particularly difficult to obtain even if our products are approved by the FDA as safe and efficacious. Patients using existing approved therapies are generally reimbursed all or part of the product cost by Medicare or other third-party payors. Medicare, Medicaid, health maintenance organizations and other third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs, and, as a result, they may not cover or provide adequate payment for these products. Submission of applications for reimbursement approval generally does not occur prior to the filing of a BLA for that product and may not be granted until many months after BLA approval. In order to obtain coverage and reimbursement for these products, we or our commercialization partners may have to agree to a net sales price lower than the net sales price we might charge in other sales channels. The continuing efforts of government and third-party payors to contain or reduce the costs of healthcare may limit our revenue. Initial dependence on the commercial success of our products may make our revenues particularly susceptible to any cost containment or reduction efforts.

Healthcare legislative reform measures intended to increase pressure to reduce prices of pharmaceutical products paid for by Medicare or, otherwise, affect the federal regulation of the U.S. healthcare system could have a material adverse effect our business, future revenue, if any, and results of operations.

In the United States, there have been a number of legislative and regulatory initiatives focused on containing the cost of healthcare. The Affordable Care Act, for example, substantially changed the way healthcare is financed by both governmental and private insurers. The Affordable Care Act contains a number of provisions that could impact our business and operations, primarily, once we obtain FDA approval to commercialize one of our product candidates in the United States, if ever, and may also affect our operations in ways we cannot currently predict. Affordable Care Act provisions that may affect our business include, among others, those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under health insurance exchanges, expansion of the 340B program, expansion of state Medicaid programs, fees and increased discount and rebate obligations, transparency and reporting requirements, and fraud and abuse enforcement. Such changes may impact existing government healthcare programs, industry competition, formulary composition, and may result in the development of new programs, including Medicare payment for performance initiatives, health technology assessments, and improvements to the physician quality reporting system and feedback program.

There have been significant ongoing judicial, administrative, executive, and legislative initiatives to modify, limit, replace, or repeal the Affordable Care Act. For example, former President Trump issued several Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Concurrently, Congress considered legislation that would repeal or replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation the Affordable Care Act have been passed. For example, the Tax Cuts and Jobs Act of 2017 eliminated the Affordable Care Act provision requiring individuals to purchase and maintain health coverage, or the "individual mandate," by reducing the associated penalty to zero, beginning in 2019. In December 2018, a district court in Texas held that the individual mandate is unconstitutional and that the rest of the Affordable Care Act is, therefore, invalid. On appeal, the Fifth Circuit Court of Appeals affirmed the holding on the individual mandate but remanded the case back to the lower court to reassess whether and how such holding affects the validity of the rest of the Affordable Care Act. The Fifth Circuit's decision on the individual mandate was appealed to the U.S. Supreme Court. On June 17, 2021, the Supreme Court held that the plaintiffs (comprised of the state of Texas, as well as numerous other states and certain individuals) did not have standing to challenge the constitutionality of the Affordable Care Act's individual mandate and, accordingly, vacated the Fifth Circuit's decision and instructed the district court to dismiss the case. As a result, the Affordable Care Act will remain in-effect in its current form for the foreseeable future; however, we cannot predict what additional challenges may arise in the future, the outcome thereof, or the impact any such actions may have on our business.

The adoption or implementation of new or amended legislation at the federal or state level could affect our ability to obtain regulatory approval for any of our vaccine candidates and the commercial viability of our future approved products, if any. We cannot predict the ultimate nature, timing, or effect of any changes to the Affordable Care Act or other federal and state reform efforts, and there is no assurance that such efforts will not adversely affect our future business and financial results.

In addition to the Affordable Care Act, there have been several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Pharmaceutical product prices have been the focus of increased scrutiny by the government, including certain state attorneys general, members of Congress and the United States Department of Justice. State or federal healthcare reform measures or other social or political pressure to lower the cost of pharmaceutical products could have a material adverse impact on our business, results of operations and financial condition.

The Biden administration also introduced various measures in 2021 focusing on healthcare and drug pricing, in particular. For example, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021, and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. On the legislative front, the American Rescue Plan Act of 2021 was signed into law on March 11, 2021, which, in relevant part, eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source drugs and innovator multiple source drugs, beginning January 1, 2024. And, in July 2021, the Biden administration released an executive order entitled, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response, on September 9, 2021, HHS released a "Comprehensive Plan for Addressing High Drug Prices" that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. And, in November 2021, President Biden announced the "Prescription Drug Pricing Plan" as part of the Build Back Better Act (H.R. 5376) passed by the House of Representatives on November 19, 2021, which aims to lower prescription drug pricing by, among other things, allowing Medicare to negotiate prices for certain high-cost prescription drugs covered under Medicare Part D and Part B after the drugs have been on the market for a certain number of years and imposing tax penalties on drug manufacturers that refuse to negotiate pricing with Medicare or increase drug prices "faster than inflation." If enacted, this bill could have a substantial impact on our business, particularly once we have commercially available products on the U.S. market, if ever. In the coming years, additional legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the potential success of our vaccine candidates.

Our relationships with customers, health care professionals and third-party payors may be subject to applicable healthcare laws, which could expose us to penalties, including administrative, civil or criminal penalties, damages, fines, imprisonment, exclusion from participation in federal healthcare programs such as Medicare and Medicaid, reputational harm, the curtailment or restructuring of our operations and diminished future profits and earnings.

Healthcare professionals and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with customers, healthcare professionals and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we conduct research, market, sell and distribute any products for which we obtain marketing approval. Federal and state healthcare laws and regulations that may affect our operations, directly or indirectly, include the following, among others:

- the federal Anti-Kickback Statute, which prohibits persons and entities from, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;

- the federal false claims laws, including civil whistleblower or qui tam actions under the federal False Claims Act, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, which imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and also imposes obligations, including mandatory contractual terms, on covered entities, including certain healthcare providers, health plans, and healthcare clearinghouses, and their respective business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of the covered entity as well as their covered subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Civil Monetary Penalties Law, which prohibits, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;

- the federal Physician Payments Sunshine Act, created under the Affordable Care Act, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually information related to certain payments or other transfers of value provided to physicians and any ownership and investment interests held by physicians or their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding payments and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year; and

- analogous state laws and regulations, including (among others) state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the United States federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information and that require tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal law, thus complicating compliance efforts.

Efforts to comply with applicable healthcare laws and regulations will involve substantial costs. Interpretations of standards of compliance under these laws and regulations are rapidly changing and subject to varying interpretations and it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other laws that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, imprisonment, additional reporting obligations and oversight (if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws), and the curtailment or restructuring of our operations, any of which could diminish our future profits or earnings. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Third-party payors may not adequately reimburse customers for any of our products that we may commercialize or promote, and may impose coverage restrictions or limitations such as prior authorizations and step edits that affect their use.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health programs, private health insurers, integrated delivery networks and other third-party payors. Third-party payors decide which medications they will pay for and establish reimbursement levels. A significant trend in the United States healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of payment for particular medications. Increasingly, third-party payors are requiring that drug companies provide predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement may not be sufficient for commercial success. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

Obtaining reimbursement approval for any product candidate for which we obtain marketing approval from any government or other third-party payor is a time-consuming and costly process. There may be significant delays in obtaining coverage and adequate reimbursement for newly approved products. Moreover, eligibility for coverage and reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Even when a payor determines that a product that we may commercialize or promote is eligible for reimbursement under its criteria, the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA, or may impose restrictions, such as prior authorization requirements, or may simply deny coverage altogether. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Coverage and reimbursement rates may vary according to the use of the drug and the medical circumstances under which it is used may be based on reimbursement levels already set for lower cost products or procedures or may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Furthermore, the Centers for Medicare and Medicaid Services frequently change product descriptors, coverage policies, product and service codes, payment methodologies and reimbursement values. Commercial third-party payors often rely upon Medicare coverage policies and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain and maintain coverage and profitable payment rates from both government-funded programs and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize our approved products and our overall financial condition.

Risks Related to Third Parties

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We do not have the ability to independently conduct our clinical trials for our product candidates and we must rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct such trials. Our reliance on these third parties for clinical development activities results in reduced control over these activities. Moreover, the FDA requires us to comply with regulations and standards, commonly referred to as GCPs (good clinical practices), for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If we or any of our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practice, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If our consultants, contract research organizations and other similar entities with which we are working do not successfully carry out their contractual duties, meet expected deadlines, or comply with applicable regulations, we may be required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, we may not be able to enter into arrangements with alternative third-party contractors or to do so on commercially reasonable terms, which may result in a delay of our planned clinical trials and delayed development of our product candidates.

In addition, our third-party contractors are not our employees, and except for remedies available to us under our agreements with such third-party contractors, we cannot control whether or not they devote sufficient time and resources to our programs. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our pre-clinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our product candidates on a timely basis, if at all, and our business, operating results and prospects would be adversely affected.

The antibodies we use in our antibody radiation-conjugate product candidates may be subject to generic competition.

We are not aware of any existing or pending regulations or legislation that pertains to generic radiopharmaceutical products such as our antibody radiation-conjugate product candidates. Our product candidates are regulated by the FDA as biologic products and we intend to seek approval for these products pursuant to the BLA pathway. The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. Even if a biosimilar gets approved for one of the antibodies that we use, the final constructs of our drug candidates consist of an antibody, radioisotope and in some cases a linker. Therefore, we do not believe that the final drug product of our candidates can be subject to competition from a biosimilar as outlined in BPCIA.

Our product candidates may never achieve market acceptance.

Iomab-B, CD33 ARC program candidates and future product candidates that we may develop may never gain market acceptance among physicians, patients and the medical community. The degree of market acceptance of any of our products will depend on a number of factors, including the actual and perceived effectiveness and reliability of the product; the results of any long-term clinical trials relating to use of the product; the availability, relative cost and perceived advantages and disadvantages of alternative technologies; the degree to which treatments using the product are approved for reimbursement by public and private insurers; the strength of our marketing and distribution infrastructure; and the level of education and awareness among physicians and hospitals concerning the product.

We believe that oncologists and other physicians will not widely adopt a product candidate unless they determine, based on experience, clinical data, and published peer-reviewed journal articles, that the use of that product candidate provides an effective alternative to other means of treating specific cancers. Patient studies or clinical experience may indicate that treatment with our product candidates does not provide patients with sufficient benefits in extension of life or quality of life. We believe that recommendations and support for the use of each product candidate from influential physicians will be essential for widespread market acceptance. Our product candidates are still in the development stage and it is premature to attempt to gain support from physicians at this time. We can provide no assurance that such support will ever be obtained. If our product candidates do not receive such support from these physicians and from long-term data, physicians may not use or continue to use, and hospitals may not purchase or continue to purchase, them.

Failure of Iomab-B, CD33 ARC program candidates or any of our other product candidates to significantly penetrate current or new markets would negatively impact our business financial condition and results of operations.

We may be subject to claims that our third-party service providers, consultants or current or former employees have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

We currently depend on single third-party manufacturers to produce our pre-clinical and clinical trial drug supplies. Any disruption in the operations of our current third-party manufacturers, or other third-party manufacturers we may engage in the future, could adversely affect our business and results of operations.

We do not currently operate manufacturing facilities for pre-clinical or clinical production of any of our product candidates. We rely on third-party manufacturers to supply, store, and distribute pre-clinical and clinical supply of the components of our drug product candidates including monoclonal antibodies, linkers and radioisotopes, as well as the final construct which comprises our drug product candidates. We expect to continue to depend on third-party manufacturers for the foreseeable future. Any performance failure on the part of our existing or future manufacturers could delay clinical development, cause us to suspend or terminate development or delay or prohibit regulatory approval of our product candidates or commercialization of any approved products. Further avenues of disruption to our clinical or eventual commercial supply may also occur due to the sale, acquisition, business reprioritization, bankruptcy or other unforeseen circumstances that might occur at any of our suppliers or contract manufacturing partners including an inability to come to terms on renewal of existing contracts or new contracts.

We currently rely on single manufacturers to manufacture our pre-clinical and clinical trial drug supplies. With a view to maintaining business continuity we are evaluating alternatives and second and even third sources of supply or manufacturing for our core suppliers and manufacturing partners, however there can be no assurances that we will be able to identify such suppliers or partners and assuming we did, that we would be able to enter into contracts that are on favorable terms or on terms that will enable sufficient supply to ensure business continuity and support our growth plans.

Our product candidates require precise, high-quality manufacturing. Failure by our current contract manufacturer or other third-party manufacturers we may engage in the future to achieve and maintain high manufacturing standards could result in patient injury or death, product recalls or withdrawals, delays or failures in testing or delivery, cost overruns, or other problems that could seriously hurt our business. Contract manufacturers may encounter difficulties involving production yields, quality control, and quality assurance. These manufacturers are subject to ongoing periodic and unannounced inspections by the FDA and corresponding state and foreign agencies to ensure strict compliance with cGMPs and other applicable government regulations and corresponding foreign standards; we do not have control over third-party manufacturers' compliance with these regulations and standards.

We may elect to build or purchase a manufacturing facility or facilities in the future to operate for the purposes of manufacturing our own products. We have never built, owned or operated a manufacturing facility. There can be no assurances that we will be able to successfully accomplish this and in doing so we may experience delays, cost overruns, or other problems that could seriously hurt our business. Even if we successfully build or purchase a manufacturing facility, we may not realize the expected benefits of these efforts.

We depend on vendors with specialized operations, equipment and know-how to manufacture the respective components of our drug candidates. We have entered into manufacturing and supply agreements with these third-parties, and in some instances, we have agreed that such vendor be the exclusive manufacturer and supplier. If any of the third-parties we depend on encounter difficulties in their operations, fail to comply with required regulations or breach their contractual obligations it may be difficult, or we may be unable to identify suitable alternative third-party manufacturers. While we identify and evaluate third-party manufacturers from time to time, even if we do identify suitable alternative third-parties, we may fail to reach agreement on contractual terms, it may be prohibitively expensive and there can be no assurance that we can successfully complete technology transfer and development work necessary or complete the necessary work in a timely manner. Any of which could prevent us from commencing manufacturing with third-parties which could cause delays or suspension of our clinical trials and pre-clinical work that may have a negative impact on our business.

Furthermore, these third-party contractors, whether foreign or domestic, may experience regulatory compliance difficulty, mechanical shut downs, employee strikes, or any other unforeseeable acts that may delay or limit production. Our inability to adequately establish, supervise and conduct (either ourselves or through third parties) all aspects of the formulation and manufacturing processes, and the inability of third-party manufacturers to consistently supply quality product when required would have a material adverse effect on our ability to develop or commercialize our products. We have faced delays and risks associated with reliance on key third party manufacturers in the past and may be faced with such delays and risks in the future. Any future manufacturing interruptions or related supply issues could have an adverse effect on our company, including delays in clinical trials.

If we are successful in obtaining marketing approval from the FDA and/or other regulatory agencies for any of our product candidates, we anticipate continued reliance on third-party manufacturers.

To date, our product candidates have been manufactured in small quantities for preclinical and clinical testing by third-party manufacturers. If the FDA or other regulatory agencies approve any of our product candidates for commercial sale, we expect that we would continue to rely, at least initially, on third-party specialized manufacturers to produce commercial quantities of approved products. These manufacturers may not be able to successfully increase the manufacturing capacity for any approved product in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. Scale-up for commercial product may require financial commitment or investment by us, which we may not have sufficient capital for or may elect not to undertake. If third party manufacturers are unable to successfully increase the manufacturing capacity for a product 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, which in turn could have a material adverse effect on our business.

In addition, the facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit a BLA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We may have conflicts with our partners that could delay or prevent the development or commercialization of our product candidates.

We may have conflicts with our partners, such as conflicts concerning the interpretation of preclinical or clinical data, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations or the ownership of intellectual property developed during our collaboration. If any conflicts arise with any of our partners, such partner may act in a manner that is averse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating revenues: unwillingness on the part of a partner to pay us milestone payments or royalties we believe are due under a collaboration; uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations; unwillingness by the partner to cooperate in the development or manufacture of the product, including providing us with product data or materials; unwillingness on the part of a partner to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities; initiating litigation or alternative dispute resolution options by either party to resolve the dispute; or attempts by either party to terminate the agreement.

We face significant competition from other biotechnology and pharmaceutical companies.

Our product candidates face, and will continue to face, intense competition from large pharmaceutical and biotechnology companies, as well as academic and research institutions. We compete in an industry that is characterized by (i) rapid technological change, (ii) evolving industry standards, (iii) emerging competition and (iv) new product introductions. Our competitors have existing products and technologies that will compete with our product candidates and technologies and may develop and commercialize additional products and technologies that will compete with our product candidates and technologies. Because several competing companies and institutions have greater financial resources than us, they may be able to (i) provide broader services and product lines, (ii) make greater investments in research and development, or R&D, and (iii) carry on broader R&D initiatives. Our competitors also have greater development capabilities than we do and have substantially greater experience in undertaking preclinical and clinical testing of product candidates, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products. They also have greater name recognition and better access to customers than us.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. Even if any of our product candidates receives marketing approval, as greater numbers of patients use a product following its approval, an increase in the incidence of side effects or the incidence of other post-approval problems that were not seen or anticipated during pre-approval clinical trials could result in a number of potentially significant negative consequences, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may elect, or we may be required, to recall or withdraw product from the market;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could substantially increase the costs and expenses of developing, commercializing and marketing any such product candidates or could harm or prevent sales of any approved products.

Risks Related to Our Intellectual Property

We depend upon securing and protecting critical intellectual property.

We are dependent on obtaining and maintaining patents, trade secrets, copyright and trademark protection of our technologies in the United States and other jurisdictions, as well as successfully enforcing this intellectual property and defending this intellectual property against third-party challenges. The degree of future protection of our proprietary rights is uncertain for product candidates that are currently in the early stages of development because we cannot predict which of these product candidates will ultimately reach the commercial market or whether the commercial versions of these product candidates will incorporate proprietary technologies.

Our patent position is highly uncertain and involves complex legal and factual questions.

Accordingly, we cannot predict the breadth of claims that may be allowed or enforced under our patents or in third-party patents. For example, we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications and issued patents; we or our licensors might not have been the first to file patent applications for these inventions; others may independently develop similar or alternative technologies or duplicate any of our technologies; it is possible that none of our pending patent applications or the pending patent applications of our licensors will result in issued patents; our issued patents and issued patents of our licensors may not provide a basis for commercially viable technologies, or may not provide us with any competitive advantages, or may be challenged and invalidated by third parties; and, we may not develop additional proprietary technologies that are patentable.

As a result, our owned and licensed patents may not be valid, and we may not be able to obtain and enforce patents and to maintain trade secret protection for the full commercial extent of our technology. The extent to which we are unable to do so could materially harm our business.

We or our licensors have applied for and will continue to apply for patents for certain products. Such applications may not result in the issuance of any patents, and any patents now held or that may be issued may not provide us with adequate protection from competition. Furthermore, it is possible that patents issued or licensed to us may be challenged successfully. In that event, if we have a preferred competitive position because of such patents, such preferred position would be lost. If we are unable to secure or to continue to maintain a preferred position, we could become subject to competition from the sale of generic products. Failure to receive, inability to protect, or expiration of our patents for medical use, manufacture, conjugation and labeling of Ac-225, the antibodies that we license from third parties, or subsequent related filings, would adversely affect our business and operations.

Patents issued or licensed to us may be infringed by the products or processes of others. The cost of enforcing our patent rights against infringers, if such enforcement is required, could be significant, and we do not currently have the financial resources to fund such litigation. Further, such litigation can go on for years and the time demands could interfere with our normal operations. There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical industry. We may become a party to patent litigation and other proceedings. The cost to us of any patent litigation, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation more effectively than we can because of their substantially greater financial resources. Litigation may also absorb significant management time.

Unpatented trade secrets, improvements, confidential know-how and continuing technological innovation are important to our scientific and commercial success. Although we attempt to and will continue to attempt to protect our proprietary information through reliance on trade secret laws and the use of confidentiality agreements with our partners, collaborators, employees and consultants and other appropriate means, these measures may not effectively prevent disclosure of our proprietary information, and, in any event, others may develop independently, or obtain access to, the same or similar information.

Certain of our patent rights are licensed to us by third parties. If we fail to comply with the terms of these license agreements, our rights to those patents may be terminated, and we will be unable to conduct our business.

If we are found to be infringing on patents or trade secrets owned by others, we may be forced to cease or alter our product development efforts, obtain a license to continue the development or sale of our products, and/or pay damages.

Our manufacturing processes and potential products may violate proprietary rights of patents that have been or may be granted to competitors, universities or others, or the trade secrets of those persons and entities. As the pharmaceutical industry expands and more patents are issued, the risk increases that our processes and potential products may give rise to claims that they infringe the patents or trade secrets of others. These other persons could bring legal actions against us claiming damages and seeking to enjoin clinical testing, manufacturing and marketing of the affected product or process. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license in order to continue to conduct clinical tests, manufacture or market the affected product or use the affected process. Required licenses may not be available on acceptable terms, if at all, and the results of litigation are uncertain. If we become involved in litigation or other proceedings, it could consume a substantial portion of our financial resources and the efforts of our personnel.

In addition to infringement or other intellectual property claims against us, we may become a party to other patent litigation or proceedings before regulatory agencies, including post-grant review, inter parties review, interference or re-examination proceedings filed with the U.S. Patent and Trademark Office (or similar proceedings before corresponding tribunals in other jurisdictions) that challenge our patent rights or the patent rights of our licensors. The costs and efforts of defending our patents or enforcing our proprietary rights in post-issuance administrative proceedings can be substantial and the outcome can be uncertain. An adverse determination in these proceedings could weaken or invalidate the patent claims that cover our technology, which adverse determination could harm our business significantly and dissuade companies from collaborating with us or permit third parties to directly compete with the same technology.

Our ability to protect and enforce our patents does not guarantee that we will secure the right to commercialize our patents.

A patent is a limited monopoly right conferred upon an inventor, and his successors in title, in return for the making and disclosing of a new and non-obvious invention. This monopoly is of limited duration but, while in force, allows the patent holder to prevent others from making and/or using its invention. While a patent gives the holder this right to exclude others, it is not a license to commercialize the invention where other permissions may be required for commercialization to occur. For example, a drug cannot be marketed without the appropriate authorization from the FDA, regardless of the existence of a patent covering the product. Further, the invention, even if patented itself, cannot be commercialized if it infringes the valid patent rights of another party.

We rely on confidentiality agreements to protect our trade secrets. If these agreements are breached by our employees or other parties, our trade secrets may become known to our competitors.

We rely on trade secrets that we seek to protect through confidentiality agreements with our employees and other parties. If these agreements are breached, our competitors may obtain and use our trade secrets to gain a competitive advantage over us. We may not have any remedies against our competitors and any remedies that may be available to us may not be adequate to protect our business or compensate us for the damaging disclosure. In addition, we may have to expend resources to protect our interests from possible infringement by others.

Risks Related to Our Operations

The use of hazardous materials, including radioactive and biological materials, in our research and development efforts imposes certain compliance costs on us and may subject us to liability for claims arising from the use or misuse of these materials.

Our research, development and manufacturing activities involve the controlled use of hazardous materials, including chemicals, radioactive and biological materials, such as radioactive isotopes. We are subject to federal, state, local and foreign environmental laws and regulations governing, among other matters, the handling, storage, use and disposal of these materials and some waste products. We cannot completely eliminate the risk of contamination or injury from these materials and we could be held liable for any damages that result, which could exceed our financial resources. We currently maintain insurance coverage for injuries resulting from the hazardous materials we use; however, future claims may exceed the amount of our coverage. Also, we do not have insurance coverage for pollution cleanup and removal. Currently the costs of complying with such federal, state, local and foreign environmental regulations are not significant, and consist primarily of waste disposal expenses. However, they could become expensive, and current or future environmental laws or regulations may impair our research, development, production and commercialization efforts.

We may undertake international operations, which will subject us to risks inherent with operations outside of the United States.

Although we do not have any international operations at this time, we intend to seek market clearances in foreign markets that we believe will generate significant opportunities. However, even with the cooperation of a commercialization partner, conducting drug development in foreign countries involves inherent risks, including, but not limited to difficulties in staffing, funding and managing foreign operations; unexpected changes in regulatory requirements; export restrictions; tariffs and other trade barriers; difficulties in protecting, acquiring, enforcing and litigating intellectual property rights; fluctuations in currency exchange rates; and potentially adverse tax consequences.

If we were to experience any of the difficulties listed above, or any other difficulties, any international development activities and our overall financial condition may suffer and cause us to reduce or discontinue our international development and registration efforts.

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

Our future operations and successes depend in large part upon the continued service of key members of our senior management team whom we are highly dependent upon to manage our business. If any member of our current senior management terminates his employment with us and we are unable to find a suitable replacement quickly, the departure could have a material adverse effect on our business. An overall tightening and increasingly competitive labor market has been observed in the U.S. employment market generally, especially in response to the COVID-19 pandemic. Specific to the biotechnology industry in which we operate, there is significant demand and competition for highly specialized talent that we require. We have experienced high turnover rates, with approximately one third of our employee base turning over or being replaced during 2021. A sustained labor shortage or increased turnover rates within our employee base, caused by the COVID-19 pandemic, as a result of general macroeconomic factors, or due to dynamics within our industry, could lead to increased costs, such as increased wage rates to attract and retain employees, and could negatively affect our ability to efficiently conduct our clinical development, R&D, business development and potential regulatory and commercial activities. If we are unable to hire and retain employees capable of performing at a high-level, or if mitigation measures we may take to respond to a decrease in labor availability, have unintended negative effects, our business could be adversely affected. An overall labor shortage, lack of skilled labor, increased turnover or labor inflation, caused by the COVID-19 pandemic, general macroeconomic factors or as a result of biotechnology industry dynamics could have a material adverse impact on our operations, results of operations, liquidity or cash flows.

Our future success also depends on our ability to identify, attract, hire or engage, retain and motivate other well-qualified managerial, technical, clinical and regulatory personnel. This activity is likely to create additional demands on the time and attention of our senior management personnel as they identify, hire, and train external and internal candidates to fill the sizable number of positions required to execute our business plans, including submitting a BLA and building a commercial organization. The market for talent in our industry is very competitive. Many of the other biopharmaceutical companies we compete against for qualified personnel have greater financial and other resources, more favorable risk profiles and a longer operating history in the biopharmaceutical industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these opportunities may be more appealing to high-quality candidates than what we have to offer.

It is particularly difficult to recruit and hire new employees during the COVID-19 pandemic as conducting interviews remotely makes it more difficult to ensure we are recruiting and hiring high-quality employees, and the uncertainty created by the COVID-19 pandemic makes it less likely potential candidates will be willing to leave a stable job to explore a new opportunity. There can be no assurance that such professionals will be available in the market, or that we will be able to retain existing professionals or meet or continue to meet their compensation requirements. Furthermore, the cost base in relation to such compensation, which may include equity compensation, may increase significantly, which could have a material adverse effect on us. Failure to establish and maintain an effective management team and workforce could adversely affect our ability to operate, grow and manage our business.

Managing our growth as we expand operations may strain our resources.

We expect to need to grow rapidly in order to support additional, larger, and potentially international, pivotal clinical trials of our product candidates as well as potential commercial operations, which will place a significant strain on our financial, managerial and operational resources. In order to achieve and manage growth effectively, we must continue to improve and expand our operational and financial management capabilities. Moreover, we will need to increase staffing and to train, motivate and manage our employees. All of these activities will increase our expenses and may require us to raise additional capital sooner than expected. Failure to manage growth effectively could materially harm our business, financial condition or results of operations.

We may expand our business through the acquisition of rights to new product candidates that could disrupt our business, harm our financial condition and may also dilute current stockholders' ownership interests in our company.

Our business strategy includes expanding our products and capabilities, and we may seek acquisitions of product candidates, antibodies or technologies to do so. Acquisitions involve numerous risks, including substantial cash expenditures; potentially dilutive issuance of equity securities; incurrence of debt and contingent liabilities, some of which may be difficult or impossible to identify at the time of acquisition; difficulties in assimilating acquired technologies or the operations of the acquired companies; diverting our management's attention away from other business concerns; risks of entering markets in which we have limited or no direct experience; and the potential loss of our key employees or key employees of the acquired companies.

We can make no assurances that any acquisition will result in short-term or long-term benefits to us. We may incorrectly judge the value or worth of an acquired product, company or business. In addition, our future success would depend in part on our ability to manage the rapid growth associated with some of these acquisitions. We cannot assure that we will be able to make the combination of our business with that of acquired products, businesses or companies work or be successful. Furthermore, the development or expansion of our business or any acquired products, business or companies may require a substantial capital investment by us. We may not have these necessary funds, or they might not be available to us on acceptable terms or at all. We may also seek to raise funds by selling shares of our preferred or common stock, which could dilute each current stockholder’s ownership interest in the Company.

Risks Related to Ownership of Our Common Stock

The sale of securities by us in any equity or debt financing could result in dilution to our existing stockholders and have a material adverse effect on our earnings.

We have financed our operations primarily through sales of stock and warrants. It is likely that during the next twelve months we will seek to raise additional capital through the sales of stock and warrants in order to expand our level of operations to continue our research and development efforts.

Any sale of common stock by us in a future offering could result in dilution to our existing stockholders as a direct result of our issuance of additional shares of our capital stock. In addition, our business strategy may include expansion through internal growth or by establishing strategic relationships with targeted customers and vendors. In order to do so, or to finance the cost of our other activities, we may issue additional equity securities that could dilute our stockholders’ stock ownership. We may also assume additional debt and incur impairment losses related to goodwill and other tangible assets if we acquire another company and this could negatively impact our earnings and results of operations.

Our common stock is subject to price volatility which could lead to losses by stockholders and potential costly security litigation.

The trading volume of our common stock has been and may continue to be extremely limited and sporadic. We expect the market price of our common stock to fluctuate substantially due to a variety of factors, including market perception of our ability to achieve our planned growth, quarterly operating results of other companies in the same industry, trading volume in our common stock, changes in general conditions in the economy and the financial markets or other developments affecting our competitors or us. This volatility has had a significant effect on the market price of securities issued by many companies for reasons unrelated to their operating performance and could have the same effect on our common stock.

The trading price of our common stock may be highly volatile and could fluctuate in response to factors such as:

- actual or anticipated variations in our operating results;
- announcements of developments by us or our competitors;
- the timing of IND and/or BLA approval, the completion and/or results of our clinical trials;
- regulatory actions regarding our products;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- adoption of new accounting standards affecting our industry;
- additions or departures of key personnel;
- introduction of new products by us or our competitors;
- sales of our common stock or other securities in the open market; and
- other events or factors, many of which are beyond our control.

The stock market is subject to significant price and volume fluctuations. Moreover, the COVID-19 pandemic has resulted in significant financial market volatility and uncertainty in recent months. In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been initiated against such a company. Litigation initiated against us, whether or not successful, could result in substantial costs and diversion of our management's attention and our resources, which could harm our business and financial condition.

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

We have never declared or paid any cash dividends on our common stock. For the foreseeable future, it is expected that earnings, if any, generated from our operations will be used to finance the growth of our business, and that no dividends will be paid to holders of our common stock. As a result, the success of an investment in our common stock will depend upon any future appreciation in its value. There is no guarantee that our common stock will appreciate in value.

Certain provisions of our Certificate of Incorporation and Bylaws and Delaware law make it more difficult for a third party to acquire us and make a takeover more difficult to complete, even if such a transaction were in our stockholders' interest.

Provisions of our certificate of incorporation and bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, the certificate of incorporation and bylaws:

- provide that the authorized number of directors may be changed by resolution of the board of directors;
- provide that all vacancies, including newly-created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide the board of directors into three classes;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and meet specific requirements as to the form and content of a stockholder's notice;

In addition, we are governed by Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a public Delaware corporation from engaging in a "business combination" with an "interested stockholder" 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. A "business combination" includes mergers, asset sales or other transactions resulting in a financial benefit to the stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years, did own, 15% or more of the corporation's outstanding voting stock. These provisions may have the effect of delaying, deferring or preventing a change in our control.

Compliance with the reporting requirements of federal securities laws can be expensive.

We are subject to the information and reporting requirements of the Exchange Act and other federal securities laws, and the compliance obligations of the Sarbanes-Oxley Act. The costs of preparing and filing annual and quarterly reports and other information with the Securities and Exchange Commission and furnishing audited reports to stockholders are substantial. In addition, we will incur substantial expenses in connection with the preparation of registration statements and related documents with respect any offerings of our common stock.

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

Our ability to utilize our federal net operating loss and tax credit carryforwards may be limited under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code. The limitations apply if we experience an "ownership change", generally defined as a greater than 50 percentage point change in the ownership of our equity by certain stockholders over a rolling three-year period. Similar provisions of state tax law may also apply. We have not assessed whether such an ownership change has previously occurred. If we have experienced an ownership change at any time since our formation, we may already be subject to limitations on our ability to utilize our existing net operating losses and other tax attributes to offset taxable income. In addition, future changes in our stock ownership, which may be outside of our control, may trigger an ownership change and, consequently, the limitations under Sections 382 and 383 of the Code. As a result, if or when we earn net taxable income, our ability to use our pre-change net operating loss carryforwards and other tax attributes to offset such taxable income may be subject to limitations, which could adversely affect our future cash flows.

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

As a public company, we operate in an increasingly demanding regulatory environment, including with respect to more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, include establishing and maintaining corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

Our compliance with Section 404 of the Sarbanes-Oxley Act requires that we incur substantial accounting expense and expend significant management efforts. We complied with Section 404 at December 31, 2021 and 2020 and while our testing did not reveal any material weaknesses in our internal controls, any material weaknesses in our internal controls in the future would be required us to remediate in a timely manner so as to be able to comply with the requirements of Section 404 each year. If we are not able to comply with the requirements of Section 404 in a timely manner each year, we could be subject to sanctions or investigations by the SEC, NYSE American or other regulatory authorities which would require additional financial and management resources and could adversely affect the market price of our common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed, and investors could lose confidence in our reported financial information.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. Multiple securities and industry analysts currently cover us. If one or more of the analysts downgrade our common stock or publish inaccurate or unfavorable research about our business, the price of our common stock would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which could cause the price of our common stock and trading volume to decline.

Our amended and restated bylaws, as amended, designate the U.S. federal district courts as the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended.

Our amended and restated bylaws, as amended, provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. In addition, our amended and restated bylaws, as amended, state that any person purchasing or otherwise acquiring any interest in our security shall be deemed to have notice of and to have consented to such provision. Such choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits, if successful, might benefit our stockholders. Stockholders who do bring a claim in the federal district courts of the United States of America could face additional litigation costs in pursuing any such claim.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 2. PROPERTIES.

We do not own any real property. We lease offices at 275 Madison Avenue, New York, NY. The lease has a term of seven years and three months, with an expiration date of September 6, 2022, with a current annual rate $342 thousand. We are also responsible for certain other costs, such as insurance, taxes, utilities and maintenance. We issued a letter of credit of $391 thousand in connection with the lease and maintained a $391 thousand certified deposit as collateral for the letter of credit. We lease lab space and offices at Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY. The lease has a term of twelve months, expiring August 31, 2022, with a current annual rate of $132 thousand.

ITEM 3. LEGAL PROCEEDINGS.

From time to time, we may become involved in various lawsuits and legal proceedings, which arise in the ordinary course of business. Litigation is subject to inherent uncertainties, and an adverse result in these or other matters may arise from time to time that may harm business. We are currently not aware of any such legal proceedings or claims that will have, individually or in the aggregate, a material adverse effect on our business, financial condition or operating results.

ITEM 4. MINE SAFETY DISCLOSURES.

Not Applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDERS MATTERS, AND ISSUER PURCHASE OF EQUITY SECURITIES.

Market Information

Our common stock is listed for quotation on the NYSE American under the symbol "ATNM".

Holders

As of March 25, 2022, there were 22,143,974 shares of common stock issued and outstanding, which were held by approximately 99 holders of record. There are no shares of preferred stock outstanding.

Dividends

We have never declared or paid any cash dividends on our common stock. For the foreseeable future, it is expected that earnings, if any, generated from our operations will be used to finance the growth of our business, and that no dividends will be paid to holders of our common stock. The decision to pay dividends is at the discretion of our board of directors and depends upon our financial condition, results of operations, capital requirements, and other factors that our board of directors deems relevant.

Securities Authorized for Issuance under Equity Compensation Plans

We currently have three equity compensation plans defined as follows:

The Company's 2019 Amended and Restated Stock Plan has an expiration date of October 18, 2029 and the number of shares of our common stock authorized under the plan for grant to employees, directors and consultants is 5,833,333 shares.

The Company's 2013 Amended and Restated Stock Plan has an expiration date of September 9, 2023 and after a number of amendments approved by stockholders, the number of shares of our common stock authorized under the plan for grant to employees, directors and consultants is 758,333 shares.

The Company's 2013 Equity Incentive Plan has an expiration date of September 9, 2023 and the number of shares of our common stock authorized under the plan for grant to employees, directors and consultants under the plan is 33,333 shares.

The following table indicates shares of common stock authorized for issuance under our equity compensation plans as of December 31, 2021:

Plan category	Number of securities to be issued upon exercise of outstanding options	Weighted-average exercise price of outstanding options	Number of securities remaining available for future issuance
Equity compensation plans approved by security holders	1,361,825	$ 12.45	5,243,242
Equity compensation plans not approved by security holders	-	-	-
Total	1,365,825	$ 12.45	5,243,242

ITEM 6. RESERVED.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATION.

The information and financial data discussed below is derived from the audited consolidated financial statements of Actinium Pharmaceuticals, Inc. for its fiscal years ended December 31, 2021 and 2020. The consolidated financial statements of Actinium Pharmaceuticals, Inc. were prepared and presented in accordance with generally accepted accounting principles in the United States. The information and financial data discussed below is only a summary and should be read in conjunction with the historical financial statements and related notes of Actinium Pharmaceuticals, Inc. contained elsewhere in this Report. The financial statements contained elsewhere in this Report fully represent Actinium Pharmaceuticals, Inc.'s financial condition and operations; however, they are not indicative of the Company's future performance. See "Cautionary Note Regarding Forward-Looking Statements" above for a discussion of forward-looking statements and the significance of such statements in the context of this Report.

Actinium Pharmaceuticals, Inc. is a clinical-stage, biopharmaceutical company applying its proprietary platform technology and deep understanding of radiobiology to the development of novel targeted radiotherapies for patients with unmet needs. Our targeted radiotherapies combine the cell-killing ability of radiation via a radioisotope payload with a targeting agent, such as a monoclonal antibody, to deliver radiation in a precise manner inside the body to specific, targeted cells, to potentially achieve greater efficacy with lower toxicity than with external beam radiation. They also enable a broader usage of radiation than external beam radiation as they can be used in the treatment of both solid tumors and blood cancers, which generally cannot be treated with external radiation given their diffuse nature. Our clinical pipeline is focused on targeting the antigens CD45 and CD33, both of which are expressed in multiple hematologic cancers, which are known to be highly sensitive to radiation. Our clinical programs are focused on two primary areas: (1) targeted conditioning prior to a bone marrow transplant ("BMT"), adoptive cell therapy ("ACT") such as CAR-T or gene therapy with Iomab-B and (2) targeted radiotherapy combinations with Actimab-A and other therapeutic agents. Our product development strategy is actively informed by clinical data with Iomab-B and Actimab-Ain approximately 600 patients, including our ongoing Pivotal Phase 3 SIERRA trial, which completed enrollment of 150 patients in the third quarter of 2021 with the last patient receiving their BMT in the fourth quarter of 2021. Our clinical pipeline has emanated from our Antibody Warhead Enabling ("AWE") technology platform, which is protected by over 170 issued and pending patents, trade secrets and know-how that we are applying to the development of targeted radiotherapies for blood and solid tumor indications independently and with collaborators. . Ongoing collaborations include a research partnership with Astellas Pharma, Inc. ("Astellas") focused on the development of theranostics for solid tumor indications, a collaboration with EpicentRx, Inc, focused on a novel CD47 immunotherapy targeted radiotherapy combination leveraging EpicentRx's RRx-01, that is being studied in a Phase 3 trial in non-small cell lung cancer, with our clinical stage Actimab-A in AML models, and a collaboration with AVEO Oncology, focused on developing a HER3 targeting ARC for solid tumors leveraging their clinical stage antibodies. We are also utilizing our AWE technology platform to advance our research objectives focused on developing next-generation targeted radiotherapies with our expanded research and development organization and research laboratories leveraging our drug development experience.

Recent Developments

Impact of COVID–19 Pandemic

The global health crisis caused by the novel coronavirus COVID-19 pandemic and its resurgences has and may continue to negatively impact global economic activity, which, despite progress in vaccination efforts, remains uncertain and cannot be predicted with confidence. In addition, the Omicron variant of COVID-19, which appears to be the most transmissible variant to date, has spread globally. The full impact of the Omicron variant, or any subsequent variant, cannot be predicted at this time, and could depend on numerous factors, including vaccination rates among the population, the effectiveness of COVID-19 vaccines against the Omicron variant and the response by governmental bodies and regulators. Given the ongoing and dynamic nature of the circumstances, it is difficult to predict the impact of the COVID-19 pandemic on our business.

Many countries around the world have continued to impose quarantines and restrictions on travel and mass gatherings to slow the spread of the virus. Accordingly, our ability to continue to operate our business may also be limited. Such events may result in a period of business, supply and drug product manufacturing disruption, and in reduced operations, any of which could materially affect our business, financial condition and results of operations. In response to COVID-19, we implemented remote working and thus far have not experienced a significant disruption or delay in our operations as it relates to the clinical development of our drug candidates. Such government-imposed precautionary measures may have been relaxed in certain countries or states, but there is no assurance that more strict measures will be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of the coronavirus, which may be more contagious and deadly than prior strains. Therefore, the COVID-19 pandemic may continue to affect our operation, may further divert the attention and efforts of the medical community to coping with COVID-19 and disrupt the marketplace in which we operate and may have a material adverse effect on our operations.

A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

We believe our earlier stage CD33 clinical trials will continue to recruit and enroll patients given the acute nature of relapsed or refractory AML. The continuation of the pandemic could adversely affect our planned clinical trial operations, including our ability to conduct the trials on the expected timelines and recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if their geography is impacted by the pandemic. Further, the continuation and/or resurgence of the COVID-19 pandemic could result in delays in our clinical trials due to prioritization of hospital resources toward the pandemic, restrictions in travel, potential unwillingness of patients to enroll in trials at this time, or the inability of patients to comply with clinical trial protocols if quarantines or travel restrictions impede patient movement or interrupt healthcare services. In addition, we rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, and the pandemic may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us, which may result in delays or hinder our ability to collect data from our clinical trials.

Additionally, COVID-19 may result in delays in receiving approvals from local and foreign regulatory authorities, delays in necessary interactions with IRB’s or Institutional Review Boards, local and foreign regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees.

To date, COVID-19 has not had a financial impact on our company. We continue to monitor the impacts of COVID-19 on the global economy and on our business operations. Although we expect that vaccinations for COVID-19 will continue to improve conditions, the ultimate impact from COVID-19 on our business operations and financial results during 2022 will depend on, among other things, the ultimate severity and scope of the pandemic, including the new variants of the virus, the pace at which governmental and private travel restrictions and public concerns about public gatherings will ease, the rate at which historically large increases in unemployment rates will decrease, if at all, and whether, and the speed with which the economy recovers. We are not able to fully quantify the impact that these factors will have on our financial results during 2022 and beyond.

Results of Operations – Year Ended December 31, 2021 Compared to the Year Ended December 31, 2020

The following table sets forth, for the periods indicated, data derived from our statements of operations:

(in thousands)	For the years ended December 31, 2021	For the years ended December 31, 2020	Increase (Decrease)
Revenue:			
Revenue	$ -	$ -	$ -
Other revenue	1,144	-	1,144
Total revenue	1,144	-	1,144
Operating expenses:			
Research and development, net of reimbursements	18,031	16,085	1,946
General and administrative	8,077	6,308	1,769
Total operating expenses	26,108	22,393	3,715
Other income			
Interest income – net	190	178	12
Total other income	190	178	12
Net loss	$ (24,774)	$ (22,215)	$ (2,559)

Revenues

We recorded no commercial revenues for the years ended December 31, 2021 and 2020, respectively.

Other revenue

We determined that certain collaborations with a third-party are within the scope of Topic ASC 606, *Revenue Recognition from Contracts with Customers,* or ASC 606. The collaboration agreement is made up of multiple modules related to various research activities. While the third party has the option to terminate the agreement at the conclusion of any module, we identified a single performance obligation to provide research services within each module for which we receive monetary consideration. We recognized revenue during the year ended December 31, 2021 of $0.9 million from these collaborations.

The National Institutes of Health awarded us a Small Business Technology Transfer cost reimbursable grant to support a clinical collaboration with Memorial Sloan Kettering Cancer Center, or MSK, to study Iomab-ACT, our CD45-targeting Antibody Radio-Conjugate, for targeted conditioning to achieve lymphodepletion prior to administration of a CD19-targeted CAR T-cell therapy developed at MSK. We recognized revenue of $0.2 million from this grant during the year ended December 31, 2021.

We recorded no other revenue for the year ended December 31, 2020.

Research and Development Expense

Research and development expenses increased by $1.9 million to $18.0 million for the year ended December 31, 2021 compared to $16.1 million for the year ended December 31, 2020. The increase was primarily due to expenses related to our research activities at our laboratory space and government grant program and higher compensation expense resulting from the hiring of additional employees.

General and Administrative Expenses

General and administrative expenses increased by $1.8 million to $8.1 million for the year ended December 31, 2021 compared to $6.3 million for the year ended December 31, 2020, primarily attributable to higher professional fees and consulting fees including recruitment costs, business taxes and fees, and insurance premiums for director and officer liability.

Other Income

Other income of $0.2 million for both time periods was attributable to interest income - net as a higher average balance of cash and cash equivalents offset a lower average interest rate.

Net Loss

Net loss increased by $2.6 million to $24.8 million for the year ended December 31, 2021 compared to $22.2 million for the year ended December 31, 2020, primarily due to higher general and administrative expenses and research and development expenses, partially offset by other revenue.

Liquidity and Capital Resources

We have financed our operations primarily through sales of our common stock, pre-funded warrants and warrants.

The following tables sets forth selected cash flow information for the periods indicated:

	For the years ended December 31,	
(in thousands)	**2021**	**2020**
Cash used in operating activities	$ (20,866)	$ (21,617)
Cash used in investing activities	(133)	(253)
Cash provided by financing activities	35,221	76,176
Net change in cash, cash equivalents and restricted cash	$ 14,222	$ 54,306

Net cash used in operating activities for the year ended December 31, 2021 of $20.9 million decreased by $0.7 million from $21.6 million for the year ended December 31, 2020, primarily due to the increased net loss of $2.6 million being more than offset by increased liabilities and increased accounts payable due to the timing of payments to vendors.

Net cash used in investing activities of $133 thousand and $253 thousand for the years ended December 31, 2021 and December 31, 2020, respectively, primarily due to the purchase of equipment for our laboratory space.

Net cash provided by financing activities for the year ended December 31, 2021 was $35.2 million, primarily from the sale of shares of our common stock. In August 2020 we entered into the Capital on Demand™ Sales Agreement with JonesTrading Institutional Services LLC, or JonesTrading, pursuant to which we may sell, from time to time, through or to JonesTrading, up to an aggregate of $200 million of our common stock. Shares of common stock are offered pursuant to our shelf registration statement on Form S-3 filed with the United States Securities and Exchange Commission, or SEC, on August 7, 2020. As of December 31, 2020, we had sold 2.1 million shares of common stock, resulting in gross proceeds of $22.6 million and net proceeds of $21.7 million. For the year ended December 31, 2021, we sold 4.6 million shares of common stock, resulting in gross proceeds of $36.5 million and net proceeds of $35.3 million.

Net cash provided by financing activities for the year ended December 31, 2020 was mainly generated by the sale of shares of common stock, pre-funded warrants and warrants. Net cash provided by financing activities was $76.2 million for the year ended December 31, 2020, reflecting $76.6 million in proceeds from the sales of common stock and pre-funded warrants in April and June 2020 and sales of common stock throughout 2020.

On April 24, 2020, we issued and sold 4.3 million shares of common stock and pre-funded warrants to purchase 2.8 million shares of common stock. The price to the public for each share of common stock sold in the offering was $4.50, and the price to the public for each pre-funded warrant sold in the offering was $4.497. The pre-funded warrants were exercisable at an exercise price of $0.003 per share and were exercisable immediately upon issuance. Gross proceeds from this offering were $31.6 million, before deducting underwriting discounts and commissions and other offering expenses payable by us. Net proceeds from the offering were approximately $29.1 million.

On June 19, 2020, we issued and sold 1.9 million shares of common stock and pre-funded warrants to purchase 0.7 million shares of common stock. The price to the public in this offering for each share of common stock was $9.75 and for each pre-funded warrant was $9.747. Each pre-funded warrant had an exercise price of $0.003 per share and were exercisable immediately upon issuance. Gross proceeds from this offering to us were $25.0 million, before deducting underwriting discounts and commissions and other offering expenses payable us. Net proceeds from this offering were approximately $23.0 million.

During the year ended December 31, 2020, holders of all 2.8 million pre-funded April 2020 warrants and 0.7 million pre-funded June 2020 warrants exercised their pre-funded warrants at $0.003 per share and received 2.8 million shares of common stock and 0.7 million shares of common stock, respectively.

We will require additional funds to conduct clinical and non-clinical trials, achieve regulatory approvals, and, subject to such approvals, commercially launch our product candidates, and will need to secure additional financing in the future to support our operations. As of the date of filing this report, we expect that our existing resources will be more than sufficient to fund our planned operations for more than 12 months following the date of this report. We base this belief on assumptions that are subject to change, and we may be required to use our available cash and cash equivalent resources sooner than we currently expect. Our actual future capital requirements will depend on many factors, including the progress and results of our ongoing clinical trials, the duration and cost of discovery and preclinical development, laboratory testing and clinical trials for our pipeline candidates, the timing and outcome of regulatory review of our product candidates, the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims and other intellectual property rights, the number and development requirements of other pipeline candidates that we pursue, and the costs of commercialization activities, including product marketing, sales, and distribution.

We expect to continue to operate at a net loss as we continue our research and development efforts, continue to conduct clinical trials and develop manufacturing, sales, marketing and distribution capabilities. There can be no assurance that the products under development by us will be approved for sale in the United States or elsewhere. Our ability to obtain additional capital may depend on prevailing economic conditions and financial, business, and other factors beyond our control. The ongoing COVID-19 pandemic has caused an unstable economic environment globally. Disruptions in the global financial markets may adversely impact the availability and cost of credit, as well as our ability to raise money in the capital markets. Current economic conditions have been, and continue to be, volatile. Continued instability in these market conditions may limit our ability to access the capital necessary to fund and grow our business.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Critical Accounting Policies

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions

Fair Value of Financial Instruments

Fair value is defined as the price that would be received to sell an asset, or paid to transfer a liability, in an orderly transaction between market participants. A fair value hierarchy has been established for valuation inputs that gives the highest priority to quoted prices in active markets for identical assets or liabilities and the lowest priority to unobservable inputs.

Revenue Recognition

We recognize revenue in accordance with ASC 606. Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration that we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue as we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to the customer.

At contract inception, once the contract is determined to be within the scope of ASC 606, we assess whether the promised goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. In determining whether goods or services are distinct, we evaluate certain criteria, including whether (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (capable of being distinct) and (ii) the good or service is separately identifiable from other goods or services in the contract (distinct in the context of the contract).

ASC 606 requires us to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in the new revenue standard as the price at which an entity would sell a promised good or service separately to a customer. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation as each performance obligation is satisfied, either at a point in time or over time, and if over time, recognition is based on the use of an output or input method.

Collaborative Arrangements

We follow the accounting guidance for collaboration agreements, which requires that certain transactions between us and collaborators be recorded in our consolidated statements of operations on either a gross basis or net basis, depending on the characteristics of the collaborative relationship, and requires enhanced disclosure of collaborative relationships. We evaluate our collaboration agreements for proper classification in our consolidated statements of operations based on the nature of the underlying activity. When we conclude that we have a customer relationship with one of our collaborators, we follow the guidance of ASC 606.

Research and Development Costs

Research and development costs are expensed as incurred. These costs include the costs of manufacturing drug components and final drug product, the costs of clinical trials, costs of employees and associated overhead, and depreciation and amortization costs related to facilities and equipment. Research and development reimbursements are recorded by us as a reduction of research and development costs.

Share-Based Payments

We estimate the fair value of each stock option award at the grant date by using the Black-Scholes option pricing model. The fair value determined represents the cost for the award and is recognized over the vesting period during which an employee is required to provide service in exchange for the award. We account for forfeitures of stock options as they occur.

Income Taxes

We use the asset and liability method to calculate deferred taxes. Deferred taxes are recognized based on the differences between the financial reporting and income tax bases of assets and liabilities using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We review deferred tax assets for a valuation allowance based upon whether it is more likely than not that the deferred tax asset will be fully realized. A valuation allowance, if necessary, is provided against deferred tax assets, based upon our assessment as to their realization.

We recognize tax when the positions meet a "more-likely-than-not" recognition threshold. There were no tax positions for which it is considered reasonably possible that the total amounts of unrecognized tax benefits will significantly increase or decrease within the next year. We recognize interest related to unrecognized tax benefits in interest expense and penalties in operating expenses.

Accounting Standards Recently Adopted

In August 2020, FASB issued ASU 2020-06, Debt—*Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*, which, among other things, provides guidance on how to account for contracts on an entity's own equity. This ASU simplifies the accounting for certain financial instruments with characteristics of liabilities and equity. Specifically, the ASU eliminated the need for us to assess whether a contract on our own equity (1) permits settlement in unregistered shares, (2) whether counterparty rights rank higher than shareholder's rights, and (3) whether collateral is required. In addition, the ASU requires incremental disclosure related to contracts on our own equity and clarifies the treatment of certain financial instruments accounted for under this ASU on earnings per share. This ASU may be applied on a full retrospective of modified retrospective basis. This ASU is effective January 1, 2022 and interim periods presented, although early adoption of this ASU was permitted effective January 1, 2021. We early adopted this standard effective January 1, 2021 and the standard did not have a significant impact on our financial statements.

Accounting Standards Recently Issued

In May 2021, FASB issued ASU 2021-04, *Earnings Per Share (topic 260), Debt — Modifications and Extinguishments (Subtopic 470-50), Compensation – Stock Compensation (Topic 718) and Derivatives and Hedging – Contracts in an Entity's Own Equity (Subtopic 815-40) – Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options*, which provides guidance of a modification or an exchange of a freestanding equity-classified written call option that remains equity classified after modification or exchange as (1) an adjustment to equity and, if so, the related earnings per share (EPS) effects, if any, or (2) an expense and, if so, the manner and pattern of recognition. The amendments in this ASU are effective January 1, 2022, including interim periods. Early adoption is permitted. We will apply the amendments prospectively to modifications or exchanges occurring on or after January 1, 2022. We will evaluate the impact of ASU 2017-09 on any future changes to the terms and conditions of its warrants.

In October 2021, FASB issued ASU 2021-08, *Business Combinations (Topic 805), Account for Contract Assets and Contract Liabilities from Contracts with Customers*, which provides guidance on accounting for contract assets and contract liabilities acquired in a business combination in accordance ASC 606. To achieve this, an acquirer may assess how the acquiree applied ASC 606 to determine what to record for the acquired revenue contracts. Generally, this should result in an acquirer recognizing and measuring the acquired contract assets and contract liabilities consistent with how they were recognized and measured in the acquiree's financial statements. The amendments of ASU 2021-08 are effective January 1, 2023, including interim periods. Early adoption is permitted, including adoption in an interim period. The Company will evaluate the impact of ASU 2021-08 on any future business combinations the Company may enter in the future.

In November 2021, the FASB issued ASU 2021-10, *Government Assistance (Topic 832), Disclosures by Business Entities about Government Assistance*, which provides guidance on disclosure requirements to entities other than not-for-profit entities about transaction with a government that are accounted for by applying a grant or contribution accounting model by analogy. ASU 2021-10 requires an entity to make annual disclosures related to (1) the nature of the transactions and the related accounting policy used to account for the government transactions, (2) quantification and disclosure of amounts related to the government transactions included in balance sheet and income statement financial statement line items, and (3) significant terms and conditions of the government transactions, including commitments and contingencies. The amendments of ASU 2021-10 are effective January 1, 2022, including interim periods. The adoption of ASU 2021-10 is not expected to have a significant impact on the Company's financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

We are not currently exposed to significant market risk related to changes in interest rates. As of December 31, 2021, our cash equivalents consisted primarily of short-term money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term nature of the cash equivalents in our portfolio and the low risk profile of our cash equivalents, an immediate 10% change in interest rates would not have a material effect on the fair market value of our financial position or results of operations.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition, or results of operations during the years ended December 31, 2021 and 2020.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of
Actinium Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Actinium Pharmaceuticals, Inc. (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations, changes in stockholders' 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 "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of 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 accounting principles generally accepted in the United States of America.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits 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 Matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ Marcum LLP

Marcum LLP

We have served as the Company's auditor since 2012**.**

Houston, Texas
March 25, 2022

Actinium Pharmaceuticals, Inc.
Consolidated Balance Sheets

(amounts in thousands, except share and per share data)	December 31, 2021	December 31, 2020
Assets		
Current Assets:		
Cash and cash equivalents	$ 77,829	$ 63,560
Restricted cash – current	392	48
Security deposit	50	-
Prepaid expenses and other current assets	1,478	1,317
Total Current Assets	79,749	64,925
Property and equipment, net of accumulated depreciation of $335 and $291	340	312
Operating lease right-of-use assets	241	579
Finance leases right-of-use assets	58	140
Security deposit	-	50
Restricted cash	-	391
Total Assets	**$ 80,388**	**$ 66,397**
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable and accrued expenses	$ 5,535	$ 4,340
Other liability	998	-
Operating leases current liability	245	342
Finance leases current liability	62	85
Total Current Liabilities	6,840	4,767
Long-term operating lease obligations	-	245
Long-term finance lease obligations	3	66
Total Liabilities	6,843	5,078
Commitments and contingencies		
Stockholders' Equity:		
Preferred stock, $0.001 par value; 50,000,000 shares authorized, 0 shares issued and outstanding	-	-
Common stock, $0.001 par value; 1,000,000,000 and 600,000,000 shares authorized; 22,143,974 and 17,532,893 shares issued and outstanding	22	18
Additional paid-in capital	329,271	292,275
Accumulated deficit	(255,748)	(230,974)
Total Stockholders' Equity	73,545	61,319
Total Liabilities and Stockholders' Equity	**$ 80,388**	**$ 66,397**

See accompanying notes to the consolidated financial statements.

Actinium Pharmaceuticals, Inc.
Consolidated Statements of Operations

(amounts in thousands, except share and per share data)	For the Year ended December 31, 2021	2020
Revenue		
Revenue	$ -	$ -
Other Revenue	1,144	-
Total revenue	1,144	-
Operating expenses:		
Research and development, net of reimbursements	18,031	16,085
General and administrative	8,077	6,308
Total operating expenses	26,108	22,393
Loss from operations	(24,964)	(22,393)
Other income:		
Interest income - net	190	178
Total other income	190	178
Net loss	**$ (24,774)**	**$ (22,215)**
Deemed dividend for warrant down-round protection provision	-	(1)
Net loss applicable to common stockholders	**$ (24,774)**	**$ (22,216)**
Net loss per common share - basic and diluted	$ (1.20)	$ (1.83)
Weighted average common shares outstanding - basic and diluted	20,568,373	12,134,259

See accompanying notes to the consolidated financial statements.

Actinium Pharmaceuticals, Inc.
Consolidated Statements of Changes in Stockholders' Equity
For the Years Ended December 31, 2021 and 2020
(amounts in thousands, except share amounts)

	Common Stock		Additional Paid-In	Accumulated	Stockholders'
	Shares	Amount	Capital	Deficit	Equity
Balance, January 1, 2020	**5,490,038**	**$ 5**	**$ 214,397**	**$ (208,758)**	**$ 5,644**
Stock-based compensation	6,262	-	1,254	-	1,254
Sale of common stock and warrants, net of offering costs	8,575,051	9	76,580	-	76,589
Issuance of common stock from exercise of pre-funded warrants	3,458,929	4	6	-	10
Issuance of common stock from exercise of warrants	2,613	-	37		37
Deemed dividend for warrant down-round protection provision	-	-	1	(1)	-
Net loss	-	-	-	(22,215)	(22,215)
Balance, December 31, 2020	**17,532,893**	**$ 18**	**$ 292,275**	**$ (230,974)**	**$ 61,319**
Stock-based compensation	21,306	-	1,694	-	1,694
Sale of common stock, net of offering costs	4,588,875	4	35,296	-	35,300
Issuance of common stock from exercise of stock options	900	-	6		6
Net loss	-	-	-	(24,774)	(24,774)
Balance, December 31, 2021	**22,143,974**	**$ 22**	**$ 329,271**	**$ (255,748)**	**$ 73,545**

See accompanying notes to the consolidated financial statements.

Actinium Pharmaceuticals, Inc.
Consolidated Statements of Cash Flows

(amounts in thousands)	**For the Year ended December 31, 2021**	**2020**
Cash Flows from Operating Activities:		
Net loss	$ (24,774)	$ (22,215)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	1,694	1,254
Depreciation and amortization expense	524	447
Changes in operating assets and liabilities:		
Decrease in:		
Prepaid expenses and other current assets	(161)	(531)
Increase (decrease) in:		
Accounts payable and accrued expenses	1,195	(257)
Other liability	998	-
Operating lease liabilities	(342)	(315)
Net Cash Used In Operating Activities	(20,866)	(21,617)
Cash Flows from Investing Activities:		
Purchase of property and equipment	(133)	(253)
Net Cash Used In Investing Activities	(133)	(253)
Cash Flows from Financing Activities:		
Payments on note payable	-	(381)
Payments on finance leases	(85)	(79)
Proceeds from sales of shares of common stock and warrants, net of offering costs	35,300	76,589
Proceeds from the exercise of stock options	6	-
Proceeds from the exercise of warrants	-	47
Net Cash Provided By Financing Activities	35,221	76,176
Net change in cash, cash equivalents and restricted cash	14,222	54,306
Cash, cash equivalents and restricted cash at beginning of year	63,999	9,693
Cash, cash equivalents and restricted cash at end of year	**$ 78,221**	**$ 63,999**
Supplemental disclosures of cash flow information:		
Cash paid for interest	$ -	$ 8
Cash paid for taxes	$ -	$ -
Supplemental disclosure of non-cash investing and financing activities:		
Deemed dividend for warrant down-round protection provision	$ -	$ 1

See accompanying notes to the consolidated financial statements.

Actinium Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements

Note 1 - Description of Business and Summary of Significant Accounting Policies

Nature of Business - Actinium Pharmaceuticals, Inc. (the "Company", "Actinium", or "We") is a clinical-stage, biopharmaceutical company focused on developing and potentially commercializing targeted radiotherapies for patients with unmet needs. The Company applies its proprietary technology platform consisting of over 170 patients, know-how and clinical experience in approximately 600 patients to develop novel therapies for blood cancer and solid tumor indications. Its clinical and preclinical development programs utilize multiple isotopes including Actinium-225, Iodine-131 and Lutetium-177 directed at multiple validated cancer targets including CD45, CD33, CD38, CD47, HER2 and HER3 for targeted conditioning prior to cell and gene therapies including bone marrow transplant and cancer therapeutics as single agents or in combination with other therapeutic modalities.

Principles of Consolidation - The consolidated financial statements include the Company's accounts and those of the Company's wholly owned subsidiaries. All significant intercompany accounts and transactions have been eliminated.

Use of Estimates in Financial Statement Presentation - The preparation of these consolidated financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Impact of COVID–19 Pandemic on Financial Statements - The global health crisis caused by the novel coronavirus ("COVID-19") pandemic and its resurgences has and may continue to negatively impact global economic activity, which, despite progress in vaccination efforts, remains uncertain and cannot be predicted with confidence. In addition, the Omicron variant of COVID-19, which appears to be the most transmissible variant to date, has spread globally. The full impact of the Omicron variant, or any subsequent variants, cannot be predicted at this time, and could depend on numerous factors, including vaccination rates among the population, the effectiveness of COVID-19 vaccines against the Omicron variant and subsequent variants and the response by governmental bodies and regulators.

Many countries around the world have continued to impose quarantines and restrictions on travel and mass gatherings to slow the spread of the virus. Accordingly, the Company's ability to continue to operate its business may also be limited. Such events may result in a period of business, supply and drug product manufacturing disruption, and in reduced operations, any of which could materially affect the Company's business, financial condition and results of operations. In response to COVID-19, the Company implemented remote working and thus far, has not experienced a significant disruption or delay in its operations as it relates to the clinical development or drug production of our drug candidates. A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on the Company's ability to access capital, which could in the future negatively affect the Company's liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect the Company's business and the value of the Company's common stock.

Additionally, COVID-19 may result in delays in receiving approvals from local and foreign regulatory authorities, delays in necessary interactions with IRB's or Institutional Review Boards, local and foreign regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees.

To date, COVID-19 has not had a financial impact on the Company. The Company continues to monitor the impacts of COVID-19 on the global economy and on its business operations. However, at this time, it is difficult to predict how long the potential operational impacts of COVID-19 will last or to what degree further disruption might impact the Company's operations and financial results.

Cash and Cash Equivalents and Restricted Cash- The Company considers all highly liquid accounts with original maturities of three months or less to be cash equivalents. Balances held by the Company are typically in excess of Federal Deposit Insurance Corporation insured limits.

Following is a summary of cash, cash equivalents and restricted cash at December 31, 2021 and December 31, 2020:

(in thousands)	December 31, 2021	December 31, 2020
Cash and cash equivalents	$ 77,829	$ 63,560
Restricted cash – current	392	48
Restricted cash – long-term	-	391
Cash, cash equivalents and restricted cash	$ 78,221	$ 63,999

Current restricted cash of $392 thousand at December 31, 2021 relates to a certificate of deposit held as collateral for a letter of credit issued in connection with the Company's lease for corporate office space. This restricted cash was classified as long-term restricted cash at December 31, 2020. Current restricted cash of $48 thousand at December 31, 2020 related to a credit card account.

Property and Equipment - Machinery and equipment are recorded at cost and depreciated on a straight-line basis over estimated useful lives of three to five years. Furniture and fixtures are recorded at cost and depreciated on a straight-line basis over estimated useful lives of seven years. When assets are retired, the cost and related accumulated depreciation are removed from the accounts, and any related gain or loss is reflected in operations. Repairs and maintenance expenditures are charged to operations. Capitalized lease assets are recorded at the lesser of the present value of minimum lease payments or fair value and amortized over the estimated useful life of the related property or term of the lease.

Leases – The Company has operating and finance leases for corporate office space, office equipment and furniture located at the corporate office space. Leases with an initial term of 12 months or less are not recorded on the balance sheet; lease expense for these leases is recognized on a straight-line basis over the lease term.

Fair Value of Financial Instruments - Fair value is defined as the price that would be received to sell an asset, or paid to transfer a liability, in an orderly transaction between market participants. A fair value hierarchy has been established for valuation inputs that gives the highest priority to quoted prices in active markets for identical assets or liabilities and the lowest priority to unobservable inputs.

Revenue Recognition - The Company recognizes revenue in accordance with Accounting Standards Codification (ASC) Topic 606, *Revenue From Contracts With Customers* ("ASC 606"). Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue as the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer.

At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses whether the promised goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. In determining whether goods or services are distinct, the Company evaluates certain criteria, including whether (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (capable of being distinct) and (ii) the good or service is separately identifiable from other goods or services in the contract (distinct in the context of the contract).

The Company then determines the transaction price, which is the amount of consideration it expects to be entitled from a customer in exchange for the promised goods or services for each performance obligation and recognizes the associated revenue as each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which it expects to be entitled. Variable consideration includes payments in the form of collaboration milestone payments. If an arrangement includes collaboration milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price.

ASC 606 requires the Company to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in the revenue standard as the price at which an entity would sell a promised good or service separately to a customer. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation as each performance obligation is satisfied, either at a point in time or over time, and if over time, recognition is based on the use of an output or input method.

Collaborative Arrangements - The Company follows the accounting guidance for collaboration agreements with third parties, which requires that certain transactions between the Company and collaborators be recorded in its consolidated statements of operations on either a gross basis or net basis, depending on the characteristics of the collaborative relationship, and requires enhanced disclosure of collaborative relationships. The Company evaluates its collaboration agreements for proper classification in its consolidated statements of operations based on the nature of the underlying activity. When the Company has concluded that it has a customer relationship with one of its collaborators, the Company follows the guidance of ASC 606.

Grant Revenue – The Company has a grant from a government-sponsored entity for research and development related activities that provide for payments for reimbursed costs, which includes overhead and general and administrative costs as well as an administrative fee. The Company recognizes revenue from grants as it performs services under this arrangement. Associated expenses are recognized when incurred as research and development expense. Revenue and related expenses are presented gross in the consolidated statements of operations.

Research and Development Costs - Research and development costs are expensed as incurred. These costs include the costs of manufacturing drug product, the costs of clinical trials, costs of employees and associated overhead, and depreciation and amortization costs related to facilities and equipment. Research and development reimbursements are recorded by the Company as a reduction of research and development costs.

Share-Based Payments - The Company estimates the fair value of each stock option award at the grant date by using the Black-Scholes option pricing model. The fair value determined represents the cost for the award and is recognized over the vesting period during which an employee is required to provide service in exchange for the award. The Company accounts for forfeitures of stock options as they occur.

Income Taxes - The Company accounts for income taxes in accordance with FASB ASC 740 Income Taxes, which requires the asset and liability method to calculate deferred taxes. Deferred taxes are recognized based on the differences between the financial reporting and income tax bases of assets and liabilities using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company reviews deferred tax assets for a valuation allowance based upon whether it is more likely than not that the deferred tax asset will be fully realized.

FASB ASC 740 prescribes guidance for the financial statement recognition, measurement and disclosure of uncertain tax positions. Tax positions must meet a "more-likely-than-not" recognition threshold to be recognized. There were no tax positions for which it is considered reasonably possible that the total amounts of unrecognized tax benefits will significantly increase or decrease within the next year. The Company recognizes interest related to unrecognized tax benefits in interest expense and penalties in operating expenses

Net Loss Per Common Share - Basic loss per common share is computed by dividing the net loss available to common stockholders by the weighted average number of common shares outstanding during the reporting period. For periods of net loss, diluted loss per share is calculated similarly to basic loss per share because the impact of all potential dilutive common shares is anti-dilutive. The Company issued pre-funded warrants in April 2020 and June 2020 that were considered outstanding shares for the purposes of calculating net loss per common share throughout 2020. As of December 31, 2020, all of the pre-funded warrants had been exercised.

For the years ended December 31, 2021 and 2020, the Company's potentially dilutive shares, which include outstanding common stock options and warrants have not been included in the computation of diluted net loss per share as the result would have been anti-dilutive.

(in thousands)	December 31, 2021	December 31, 2020
Options	1,362	815
Warrants	2,112	2,113
Total	3,474	2,928

Subsequent Events - The Company's management reviewed all material events through the date the consolidated financial statements were issued for subsequent event disclosure consideration.

Accounting Standards Recently Adopted - In August 2020, FASB issued ASU 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*, which, among other things, provides guidance on how to account for contracts on an entity's own equity. This ASU simplifies the accounting for certain financial instruments with characteristics of liabilities and equity. Specifically, the ASU eliminated the need for the Company to assess whether a contract on the entity's own equity (1) permits settlement in unregistered shares, (2) whether counterparty rights rank higher than shareholder's rights, and (3) whether collateral is required. In addition, the ASU requires incremental disclosure related to contracts on the entity's own equity and clarifies the treatment of certain financial instruments accounted for under this ASU on earnings per share. This ASU may be applied on a full retrospective of modified retrospective basis. This ASU is effective January 1, 2022 and interim periods presented, although early adoption of this ASU was permitted effective January 1, 2021. The Company early adopted this standard effective January 1, 2021 and the standard did not have a significant impact on the Company's financial statements.

Accounting Standards Recently Issued– In May 2021, FASB issued ASU 2021-04, *Earnings Per Share (topic 260), Debt — Modifications and Extinguishments (Subtopic 470-50), Compensation – Stock Compensation (Topic 718) and Derivatives and Hedging – Contracts in an Entity's Own Equity (Subtopic 815-40) – Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options*, which provides guidance of a modification or an exchange of a freestanding equity-classified written call option that remains equity classified after modification or exchange as (1) an adjustment to equity and, if so, the related earnings per share (EPS) effects, if any, or (2) an expense and, if so, the manner and pattern of recognition. The amendments in this ASU are effective January 1, 2022, including interim periods. Early adoption is permitted. The Company will apply the amendments prospectively to modifications or exchanges occurring on or after January 1, 2022. The Company will evaluate the impact of ASU 2017-09 on any future changes to the terms and conditions of its warrants.

In October 2021, FASB issued ASU 2021-08, *Business Combinations (Topic 805), Account for Contract Assets and Contract Liabilities from Contracts with Customers*, which provides guidance on accounting for contract assets and contract liabilities acquired in a business combination in accordance with ASC 606. To achieve this, an acquirer may assess how the acquiree applied ASC 606 to determine what to record for the acquired revenue contracts. Generally, this should result in an acquirer recognizing and measuring the acquired contract assets and contract liabilities consistent with how they were recognized and measured in the acquiree's financial statements. The amendments of ASU 2021-08 are effective January 1, 2023, including interim periods. Early adoption is permitted, including adoption in an interim period. The Company will evaluate the impact of ASU 2021-08 on any future business combinations the Company may enter in the future.

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Note 2 - Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following at December 31, 2021 and 2020:

	December 31, 2021	December 31, 2020
Prepaid insurance	$ 874	$ 792
Prepaid clinical trial expenses	543	457
Other prepaid expenses and other current assets	61	68
Total prepaid expenses and other current assets	$ 1,478	$ 1,317

Note 3 - Property and Equipment

Property and equipment consisted of the following at December 31, 2021 and 2020:

(in thousands)	Lives	December 31, 2021	December 31, 2020
Lab equipment	5 years	$ 476	$ 378
Office equipment and furniture	3 - 7 years	199	225
Less: accumulated depreciation		(335)	(291)
Property and equipment, net		$ 340	$ 312

Depreciation expense consisted of the following for the years ended December 31, 2021 and 2020, respectively:

(in thousands)	December 31, 2021	December 31, 2020
Research and development	$ 88	$ 36
General administrative	17	18
Total Depreciation expense	$ 105	$ 54

Note 4 - Leases

The Company determines if an arrangement is a lease at inception. This determination generally depends on whether the arrangement conveys to the Company the right to control the use of a fixed asset for a period of time in exchange for consideration. Control of an underlying asset is conveyed to the Company if the Company obtains the rights to direct the use of and to obtain substantially all of the economic benefits from using the underlying asset. The Company has lease agreements which include lease and non-lease components, which the Company has elected to account for as a single lease component for all classes of underlying assets. Lease expense for variable lease components are recognized when the obligation is probable. The Company made an accounting policy election to exclude from balance sheet reporting those leases with initial terms of 12 months or less.

Right-of-use assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. ASC 842 requires a lessee to discount its unpaid lease payments using the interest rate implicit in the lease or, if that rate cannot be readily determined, its incremental borrowing rate. As an implicit interest rate was not readily determinable in the Company's leases, the incremental borrowing rate was used based on the information available at commencement date in determining the present value of lease payments.

The lease term for all of the Company's leases includes the non-cancellable period of the lease plus any additional periods covered by either a Company option to extend (or not to terminate) the lease that the Company is reasonably certain to exercise, or an option to extend (or not to terminate) the lease controlled by the lessor. Options for lease renewals have been excluded from the lease term (and lease liability) for the majority of the Company's leases as the reasonably certain threshold is not met.

At December 31, 2021, the Company has an operating lease for corporate office space and two finance leases for office equipment and furniture located in the corporate office space. In addition, the Company has auxiliary corporate office space that it rents on a month-to-month basis; this rental is accounted for as an operating lease with the same term as the Company's main office in the same building.

The components of lease expense are as follows:

(in thousands)	Year ended December 31, 2021	Year ended December 31, 2020
Operating lease expense	$ 372	$ 372
Finance lease cost		
Amortization of right-to-use assets	$ 81	$ 81
Interest on lease liabilities	$ 9	$ 16
Total finance lease cost	90	$ 97

Supplemental cash flow information related to leases are as follows:

	Year ended	
(in thousands)	December 31, 2021	December 31, 2020
Cash flow information:		
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flow use from operating leases	$ 377	$ 375
Operating cash flow use from finance leases	$ 9	$ 16
Financing cash flow use from finance leases	$ 85	$ 78
Non-cash activity:		
Right-of-use assets obtained in exchange for lease obligations:		
Operating leases	$ -	$ 83
Finance Leases	$ -	$ -

Weighted average remaining lease terms are as follows at December 31, 2021:

Weighted average remaining lease term:	
Operating leases	0.6 years
Finance Leases	0.8 years

As the interest rate implicit in the leases was not readily determinable at the time that the leases were evaluated, the Company used its incremental borrowing rate based on the information available in determining the present value of lease payments. The Company's incremental borrowing rate was based on the term of the lease, the economic environment of the lease and reflect the rate the Company would have had to pay to borrow on a secured basis. Below is information on the weighted average discount rates used at the time that the leases were evaluated:

Weighted average discount rates:	
Operating leases	8%
Finance Leases	8%

Maturities of lease liabilities are as follows:

Year ending December 31,		Operating Leases		Finance Leases
2022		252		64
2023		-		4
Total lease payments	$	252	$	68
Less imputed interest		(7)		(3)
Present value of lease liabilities	$	245	$	65

Note 5 - Other revenue

The Company has a grant from a government-sponsored entity for research and development related activities that provide for payments for reimbursed costs, which includes overhead and general and administrative costs as well as an administrative fee. The Company recognizes revenue from grants as it performs services under this arrangement. Associated expenses are recognized when incurred as research and development expense. Revenue of $0.2 million was recognized during year ended December 31, 2021.

The Company determined that certain collaborations with a third-party are within the scope of ASC 606. The collaboration agreement is made up of multiple modules related to various research activities. The Company identified a single performance obligation to provide research services within each module for which the Company receives monetary consideration. The third-party can choose to proceed with each module or can terminate the agreement at any time. The Company recognizes revenue for each module on a straight-line basis over the expected module period. Revenue for succeeding modules is not recognized until all contingencies are resolved, inclusive of the third-party's ability to terminate the module. The consideration is recognized to revenue over each module and revenue recognized during the year ended December 31, 2021 was $0.9 million. Other liability consists of $1.0 million of deferred other revenue that is expected to be recognized during 2022.

Note 6 - Commitments and Contingencies

On June 15, 2012, the Company entered into a license and sponsored research agreement with Fred Hutchinson Cancer Research Center ("FHCRC") to build upon previous and ongoing clinical trials with apamistamab (licensed antibody). FHCRC has completed both a Phase 1 and Phase 2 clinical trial with apamistamab. The Company has been granted exclusive rights to the antibody and related master cell bank developed by FHCRC. A milestone payment of $1 million will be due to FHCRC upon FDA approval of the first drug utilizing the licensed antibody. Upon commercial sale of the drug, royalty payments of 2% of net sales will be due to FHCRC.

Note 7 - Equity

On April 24, 2020, the Company issued and sold 4.3 million shares of common stock and 2.8 million pre-funded warrants to purchase shares of common stock. The price to the public in this offering for each share of common stock was $4.50 and for each pre-funded warrant was $4.497. Each pre-funded warrant had an exercise price of $0.003 per share and was exercisable immediately upon issuance. Gross proceeds from this offering were $31.6 million, before deducting underwriting discounts and commissions and other offering expenses payable by the Company. Net proceeds from this offering were $29.1 million.

During the year ended December 31, 2020, holders of all of the 2.8 million pre-funded April 2020 warrants exercised their warrants at $0.003 per share and received 2.8 million shares of common stock.

On June 19, 2020, the Company issued and sold 1.9 million shares of common stock and 0.7 million pre-funded warrants to purchase shares of common stock. The price to the public in this offering for each share of common stock was $9.75 and for each pre-funded warrant was $9.747. Each pre-funded warrant had an exercise price of $0.003 per share and was exercisable immediately upon issuance. Gross proceeds from this offering were $25.0 million, before deducting underwriting discounts and commissions and other offering expenses payable by the Company. Net proceeds from this offering were $23.0 million.

During the year ended December 31, 2020, holders of all of the 0.7 million pre-funded June 2020 warrants exercised their warrants at $0.003 per share and received 0.7 million shares of common stock.

In August 2020, the Company entered into the Capital on Demand™ Sales Agreement with JonesTrading Institutional Services LLC ("JonesTrading"), pursuant to which the Company may sell, from time to time, through or to JonesTrading, up to an aggregate of $200 million of its common stock. Shares of common stock are offered pursuant to the Company's shelf registration statement on Form S-3 filed with the SEC on August 7, 2020. As of December 31, 2020, the Company had sold 2.1 million shares of common stock, resulting in gross proceeds of $22.6 million and net proceeds of $21.7 million. For the year ended December 31, 2021, the Company sold 4.6 million shares of common stock, resulting in gross proceeds of $36.5 million and net proceeds of $35.3 million.

2019 Amended and Restated Stock Plan

In December 2019, the Company's 2019 Stock Plan was established. The expiration date of the plan is October 18, 2029 and the total number of shares of the Company's common stock available for grant to employees, directors and consultants of the Company was 333,333 shares. At the Company's Annual Meeting of Stockholders held on November 18, 2020, its stockholders authorized an increase in the number of shares authorized under the plan, resulting in the number of shares authorized in the plan to be 3,083,333 shares. At the Company's Annual Meeting of Stockholders held on November 9, 2021, its stockholders authorized an increase in the number of shares authorized under the plan, resulting in the number of shares authorized in the plan to be 5,833,333 shares.

2013 Amended and Restated Stock Plan

In September 2013, the Company's 2013 Stock Plan was established. The expiration date of the plan is September 9, 2023 and at the time of approval, the total number of shares of the Company's common stock available for grant to employees, directors and consultants of the Company under the plan was 91,666 shares. After a number of amendments approved by stockholders, the number of shares authorized under the plan is 758,333 shares.

2013 Equity Incentive Plan

In September 2013, the Company's 2013 Equity Incentive Plan was established. The expiration date of the plan is September 9, 2023 and the total number of shares of the Company's common stock available for grant to employees, directors and consultants of the Company under the plan was 15,000 shares. In December 2013, the shareholders of the Company approved the plan and increased the number of shares authorized under the plan to 33,333 shares.

Stock Options

Following is a summary of stock option activity for the years ended December 31, 2021 and 2020:

(in thousands, except for per-share amount)	**Number of Options**	**Weighted Average Exercise Price**	**Weighted Average Remaining Contractual Term (in years)**	**Aggregate Intrinsic Value at December 31, 2021**
Outstanding, January 1, 2020	380	35.10	7.88	155
Granted	458	9.99		
Cancelled	(23)	16.84		
Outstanding, December 31, 2020	815	21.53	8.51	120
Granted	881	6.43		
Exercised	(1)	6.69		
Cancelled	(333)	18.78		
Outstanding, December 31, 2021	1,362	12.45	8.69	-
Exercisable, December 31, 2021	354	27.04	6.92	-

During 2021, the Company granted its employees and members of the Board of Directors options to purchase 881 thousand shares of common stock with an exercise price ranging from $6.02 to $9.25 per share, a term of 10 years, and a vesting period from 4 to 4.2 years. The options have an aggregated fair value of $3.9 million that was calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate range from 0.65% to 1.28% (2) expected life of 6 years, (3) expected volatility range from 79.8% to 85.1%, and (4) zero expected dividends.

During 2020, the Company granted its employees and members of the Board of Directors options to purchase 458 thousand shares of common stock with an exercise price ranging from $6.63 to $12.41 per share, a term of 10 years, and a vesting period from 4 to 4.2 years. The options have an aggregated fair value of $3.2 million that was calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate range from 0.34% to 0.56% (2) expected life of 6 years, (3) expected volatility range from 83.6% to 85.5%, and (4) zero expected dividends.

During the years ended December 31, 2021 and 2020, options to purchase 333 thousand and 23 thousand common shares were cancelled, respectively, upon the termination of employment. During 2021, 1 thousand options were exercised for shares of common stock. There were no exercises of options during 2020.

The fair values of all options issued and outstanding are being amortized over their respective vesting periods. The unrecognized compensation expense at December 31, 2021 was $4.9 million related to unvested options, which is expected to be expensed over a weighted average of 3.3 years. During 2021 and 2020, the Company recorded total option expense of $1.5 million and $1.2 million, respectively.

Pre-funded Warrants

As part of the April 2020 offering and the June 2020 offering, the Company issued pre-funded warrants. Each pre-funded warrant had an exercise price of $0.003 per share and was exercisable immediately upon issuance. The pre-funded warrants did not have an expiration date. During 2020 all the pre-funded warrants were exercised for shares of common stock.

Warrants

Following is a summary of warrant activities for the years ended December 31, 2021 and 2020:

(in thousands, except for per-share amounts)	Number of Warrants	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding, January 1, 2020	2,871	20.71	2.95	301
Granted	-	-		
Exercised	(2)	15.00		
Cancelled	(756)	20.99		
Outstanding, December 31, 2020	2,113	20.55	2.76	362
Granted	1	8.30		
Exercised	-	-		
Cancelled	(2)	50.17		
Outstanding, December 31, 2021	2,112	20.52	1.76	276
Exercisable, December 31, 2021	2,108	20.12	1.76	276

The Company has an outstanding warrant to purchase 1,907 shares of common stock, issued on March 14, 2017 to Sandesh Seth, the Company's Chairman and Chief Executive Officer. The warrant included down-round protection up until it was amended on August 11, 2020. For warrants with down-round protection, a deemed dividend is recorded for the change in fair value of the warrants when the down-round provision is triggered. As a result of the April 2020 offering and June 2020 offering, the exercise price of the warrant was reset from $26.40 per share to $15.62 per share. The down-round protection provision in the above warrants created a deemed dividend to common stockholders of $1 thousand in the year ended December 31, 2020 which is reflected in the accompanying consolidated statement of operations and consolidated statement of changes in stockholders' equity. On August 11, 2020, the Company and Mr. Seth agreed to amend the warrant to remove the anti-dilution provision that had been in the warrant. Accordingly, pursuant to the amendment, as of August 11, 2020, the exercise price of the warrant will no longer be subject to a proportional adjustment if and when the Company issues any shares of its common stock for a consideration less than the exercise price of the warrant. All other terms of the warrant remained the same.

During the years ended December 31, 2021 and 2020, the Company recorded stock-based compensation expense related to warrants of $16 thousand and $13 thousand, respectively.

Note 8 - Income Taxes

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and liabilities at December 31, 2021 and 2020 are as follows:

(in thousands)	**2021**	**2020**
Deferred tax assets:		
Net operating losses carry forward	$ 36,405	$ 33,955
Share-based compensation	1,213	1,689
Research and development/orphan drug credits	14,536	12,638
Intangibles	10,426	7,873
Others	19	19
Less: valuation allowance	(62,599)	(56,174)
Deferred tax assets, net	$ -	$ -

The Company has recorded a valuation allowance of $62.6 million and $56.2 million against its deferred tax assets at December 31, 2021 and 2020 respectively, because management determined that it is not more-likely-than not that those assets will be realized.

For federal income tax purposes, the Company has $163.0 million of unused net operating losses ("NOLs") at December 31, 2021 available for carry forward to future years. NOLs of $120.8 million generated prior to 2018 will begin to expire if unused in 2022. NOLs generated in 2018 and later years of $42.2 million have an indefinite life, but will be limited to 80% of their value if used in a tax year ending after January 1, 2022.

For state income tax purposes, the Company has $87.9 million of unused NOLs at December 31, 2021 available for carry forward to future years. These NOLs will begin to expire in 2034 if unused.

The Company has federal research and development tax credits of $2.9 million at December 31, 2021 which will begin to expire in 2034 if unused and orphan drug credits of $11.6 million which will begin to expire in 2028 if unused.

Federal and state tax laws impose limitations on the utilization of net operating losses and credit carryforwards in the event of an ownership change for tax purposes, as defined in Section 382 of the Internal Revenue Code. Accordingly, the Company's ability to utilize these carryforwards may be limited as a result of an ownership change which may have already happened or may happen in the future. Such an ownership change could result in a limitation in the use of the net operating losses in future years and possibly a reduction of the net operating losses available.

The difference between the income tax provision and the amount that would result if the U.S. Federal statutory rates were applied to pre-tax losses for the year ended December 31, 2021 and 2020 are as follows:

(in thousands)	**December 31, 2021**		**December 31, 2020**	
Federal statutory income taxes	$ (5,202)	(21.0)%	$ (4,665)	(21.0)%
State income taxes	(373)	(1.5)%	56	0.3%
Deferred true-up	562	2.3%	(64)	(0.3)%
Research and development/orphan drug tax credit	(1,898)	(7.7)%	(1,766)	(8.0)%
Other	486	2.0%	202	0.9%
Change in valuation allowance	6,425	25.9%	6,237	28.1%
Provision for income tax	$ -	-	$ -	-

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

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Disclosure controls and procedures. The Company, under the supervision and with the participation of its management, including the Company's principal executive officer and principal financial and accounting officer, evaluated the effectiveness of the Company's "disclosure controls and procedures," as such term is defined in Rule 13a-15(e) and 15d-15(e) under the Securities Act of 1934, as amended (the "Exchange Act"), as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, the Company's principal executive officer and principal financial and accounting officer have concluded that the Company's disclosure controls and procedures are effective as of December 31, 2021 to ensure that information required to be disclosed by the Company in reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission rules and forms, and includes controls and procedures designed to ensure that information required to be disclosed by the Company in such reports is accumulated and communicated to the Company's management, including the Company's principal executive officer and principal financial and accounting officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control Over Financial Reporting. The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting. The Company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

The Company's internal control over financial reporting includes policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect transactions and dispositions of assets; (2) provide reasonable assurances that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with authorizations of management and the directors of the Company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's 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. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2021. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013). Based on its assessment and those criteria, management concluded that as of December 31, 2021, the Company's internal control over financial reporting was effective.

This Annual Report on Form 10-K does not include an attestation report from our registered public accounting firm regarding internal control over financial reporting. Our internal control over financial reporting was not subject to such attestation as we are a non-accelerated filer.

***Changes in internal controls over financial reporting*.** There were no changes in the Company's internal controls over financial reporting that occurred during the fourth quarter of the fiscal year covered by this Annual Report on Form 10-K that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

ITEM 9B. OTHER INFORMATION.

Item 5.03 Amendments to Articles of Incorporation or Bylaws; Change in Fiscal Year.

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

Directors and Executive Officers

The names, positions and ages of our directors and executive officers as of March 25, 2022, are as follows:

Name	Age	Position
Sandesh Seth	57	Chairman and Chief Executive Officer
Steve O'Loughlin	37	Chief Financial Officer (Principal Financial and Accounting Officer)
Jeffrey W. Chell M.D.	67	Director
David Nicholson, Ph.D.	66	Lead Independent Director
Richard I. Steinhart	64	Director
Ajit S. Shetty, Ph.D.	75	Director

Subject to the classified board provisions of our Charter, all directors hold office until the next annual meeting of stockholders and the election and qualification of their successors. Officers are elected annually by the Board of Directors and serve at the discretion of the Board of Directors.

There are no other arrangements or understanding between any of our directors and any other persons pursuant to which they were selected as a director.

Background of Executive Officers and Directors

The principal occupations for the past five years (and, in some instances, for prior years) of each of our directors and executive officers are as follows:

Sandesh Seth, Chairman and Chief Executive Officer

Mr. Sandesh Seth has been our Chief Executive Officer since June 2017. Mr. Seth has been a Director since March 2012, our Chairman of the Board since October 2013, and served as Executive Chairman from August 2014 to June 2017.

Mr. Seth has 25+ years of experience in investment banking (Laidlaw& Co (UK) Ltd., Cowen & Co.), equity research (Bear Stearns, Commonwealth Associates) and in the pharma industry (Pfizer, Warner-Lambert, SmithKline in strategic planning, business development and R&D project management). Mr. Seth was chairman of Relmada Therapeutics Inc., a specialty pharma company focused on CNS therapeutics, which he helped co-found. Mr. Seth has an MBA in Finance from New York University; an M.S. in the Pharmaceutical Sciences from the University of Oklahoma Health Center and a B.Sc. in Chemistry from Bombay University. He has published several scientific articles and was awarded the University Regents Award for Research Excellence at the University of Oklahoma. Mr. Seth was designated as Regulatory Affairs Certified by the Regulatory Affairs Professionals Society which signifies proficiency with U.S. FDA regulations. He has several patents related to use of radiopharmaceuticals as conditioning agents for adoptive cell therapies and as therapeutic combinations.

That Mr. Seth has served in various business executive-level positions over the course of his career, has significant investment banking experience, has developed significant management, operational and leadership skills and is well accustomed to interfacing with investors, analysts, auditors, C-level executives, and outside advisors, led us to conclude that Mr. Seth should serve as a director.

Steve O'Loughlin, Chief Financial Officer

Steve O'Loughlin has been our Chief Financial Officer since August 2020. Mr. O'Loughlin served as our Principal Financial Officer from May 2017 to August 2020. Mr. O'Loughlin joined Actinium in October 2015 as Vice President, Finance and Corporate Development, with almost a decade of life sciences industry experience gained from previous positions in investment banking and publicly traded life sciences companies. Prior to Actinium, from June 2015 to October 2015, Mr. O'Loughlin worked at J. Streicher LLC as an investment banker, from August 2012 to June 2015 Mr. O'Loughlin held the position of vice president, corporate finance and development and was a corporate officer at Protea Biosciences, Inc., a publicly traded life sciences tools company. Previously, From June 2010 to June 2012, Mr. O'Loughlin held corporate development positions with Caliber I.D., a publicly traded diagnostics company. Mr. O'Loughlin previously worked in investment banking at Jesup & Lamont where he focused on the biotechnology and life sciences industries. Mr. O'Loughlin has a B.S. in Business Administration with a concentration in finance from Ramapo College of New Jersey.

Jeffrey W. Chell, M.D., Director

Dr. Chell has been a Director of the Company since April 2018. Dr. Chell is also a member of our Audit Committee and Compensation Committee. He has been the chief executive officer emeritus of the National Marrow Donor Program ("NMDP") since 2017 having served as its chief executive officer since 2000. Dr. Chell has led the NMDP through transformational growth as its Be The Match Registry tripled to more than 12 million donors, the number of transplants facilitated has grown fivefold to over 6,400 annually, and revenue more than tripled to nearly $400 million per year. He is also the co-founder and has served as executive director of the Center For International Blood & Marrow Transplant Research since 2004, a leading research program in the field contributing over 70 research publications per year in peer-reviewed journals. Dr. Chell also currently serves as chair of CLR Insurance, a captive insurance company domiciled in the Cayman Islands. From 2014 to 2016, Dr. Chell served as co-chair of Bone Marrow Donors Worldwide during its IT transformation project, improving revenues and reducing costs.

Prior to joining the NMDP, he served as president, Allina Medical Clinics, a 450 physician multi-specialty medical group from 1994 to 1999. Prior to that he practiced Internal Medicine in Minneapolis and in the U.S. Air Force Medical Corps.

Dr. Chell received his M.D. from the University of Minnesota and his training in Internal Medicine at the University of Wisconsin, Madison. Dr. Chell is a diplomate of the American Board of Internal Medicine, a member of the American Society of Hematology and a member of the American Society of Blood and Marrow Transplantation.

He has received multiple honors including the 2018 Public Service award of the American Society For Blood and Marrow Transplantation, 2017 Most Admired CEO by the Minneapolis/St. Paul Business Journal, 2010 Healthcare Executive of the Year by the Minneapolis/St, Paul Business Journal, and the 2017 Bone Marrow Foundation Service Award.

That Dr. Chell brings many years of experience with patient donor programs, knowledge of challenges related to bone marrow transplants, leadership of organizations and experience working in medical groups to our Board, led us to conclude that Dr. Chell should serve as a director.

David Nicholson, Ph.D., Director

David Nicholson has been a Director of the Company since 2008. Dr. Nicholson is also a member of our Compensation Committee and Corporate Governance Committee. Since March 2015, Dr. Nicholson served as Executive Vice President and Chief R&D Officer of Allergan, which was acquired by Abbvie in May 2020. In August 2014, Dr. Nicholson joined Allergan (previously known as Actavis plc and Forest Laboratories, Inc.) as senior vice president, Actavis Global Brands R&D. From March 2012 to August 2014, Dr. Nicholson was on the executive committee of Bayer CropScience as head of research & development responsible for the integration of the company's R&D activities into one global organization. Dr. Nicholson graduated in pharmacology, earning his B.Sc. from the University of Manchester (1975) and his Ph.D. from the University of Wales (1980). Between 1978 and 1988, Dr. Nicholson worked in the pharmaceutical industry for the British company Beecham-Wülfing in Gronau, Germany. The main emphasis of his activities as group leader in a multidisciplinary project group was the development of cardiovascular drugs.

From 1988-2007, Dr. Nicholson held various positions of increasing seniority in the UK, the Netherlands and the U.S. with Organon, a business unit of Akzo Nobel. Ultimately, he became executive vice president, research & development, and member of the Organon Executive Management Committee. He implemented change programs, leading to maximizing effectiveness in research & development, ensuring customer focus and the establishment of a competitive pipeline of innovative drugs. In 2007, Dr. Nicholson transferred to Schering-Plough, Kenilworth, New Jersey as senior vice president, responsible for Global Project Management and Drug Safety. From 2009 to December 2011, he was vice president licensing and knowledge management at Merck in Rahway, New Jersey, reporting to the president of Merck R&D. As an integration team member, Dr. Nicholson played a role in the strategic mergers of Organon BioSciences, the human and animal health business of Dutch chemical giant Akzo-Nobel, and Schering-Plough in 2007 as well as of Schering-Plough and Merck in 2009.

That Dr. Nicholson brings over 25 years of pharmaceutical experience to our Board, having served in various pharmaceutical research and development executive-level positions over the course of his career, and that Dr. Nicholson has developed significant management and leadership skills relating to the pharmaceutical industry. and is well accustomed to interfacing with investors, analysts, auditors, outside advisors and governmental officials, led us to conclude that Dr. Nicholson should serve as a director.

Ajit S. Shetty, Ph.D., Director

Dr. Shetty has been a Director of the Company since March 2017. Dr. Shetty is also a member of our Audit Committee, Compensation Committee, and Chairman of our Corporate Governance Committee. Dr. Shetty joined Janssen Pharmaceutical, Inc. ("Janssen") in 1976 ultimately rising to the position of president in 1986 where he led the establishment of Janssen's business in the U.S. From 1999 to 2008 he was managing director of Janssen, during this time the Janssen Group of companies' global sales grew from $1 billion to $8 billion, and from 2004 until 2012 he was chairman of the board of directors. In Dr. Shetty's most recent role at Johnson & Johnson he was head of Enterprise Supply Chain, where he reported to the chief executive officer and was responsible for the transformation and optimization of Johnson & Johnson's supply chain. Dr. Shetty earned a Ph.D. in Metallurgy and B.A. Natural Sciences from Trinity College, Cambridge University and a Master of Business Administration from Carnegie Mellon University. Dr. Shetty has served as a member of Agile Therapeutics, Inc.'s board of directors since February 2016. In 2007, Dr. Shetty was bestowed the title of Baron by King Albert II of Belgium for his exceptional merits. He is a member of the Board of Trustees of Carnegie Mellon University, serves on the Board of Governors for GS1 (Global Standards) in Belgium and formerly served on the Corporate Advisory Board of the John Hopkins Carey Business School. In 2016, Dr. Shetty was named as chairperson of the Vlaams Instituut voor Biotechnologie (VIB), a Belgium based life sciences research institute focused on translating scientific results into pharmaceutical, agricultural and industrial applications. In addition, he was elected Manager of the Year in 2004 in Flanders and received a Life-Time Achievement Award in India in 2010. We believe Dr. Shetty's qualifications to sit on our Board include his extensive pharmaceutical experience leading commercial and supply chain operations and his significant education background.

That Dr. Shetty has 37 years of leadership and executive experience in the pharmaceutical industry, that he has significant supply chain knowledge and that he has experience conducting business in the U.S. and Europe, led us to conclude that Dr. Shetty should serve as a director.

Richard I. Steinhart, Director

Mr. Steinhart has served as our Director and Chairman of the Audit Committee since November 2013. Mr. Steinhart is also a member of our Corporate Governance Committee. Since October 2017 Mr. Steinhart has been the senior vice president and chief financial officer of BioXcel Therapeutics, Inc. Since March 2014, Mr. Steinhart has been a member of the board of directors of Atossa Genetics, Inc. where he is chairman of the audit committee and a member of the compensation committee. From October 2015 to April 2017, Mr. Steinhart was vice president and chief financial officer at Remedy Pharmaceuticals, a privately-held, clinical stage pharmaceutical company. From January 2014 through September 2015 Mr. Steinhart worked as a financial and strategic consultant to the biotechnology and medical device industries. From April 2006 through December 2013, Mr. Steinhart was employed by MELA Sciences, Inc., as its vice president, finance and chief financial officer, treasurer and secretary. In April 2012, Mr. Steinhart received a promotion to senior vice president, finance and chief financial officer. From May 1992 until joining MELA Sciences, Mr. Steinhart was a managing director of Forest Street Capital/SAE Ventures, a boutique investment banking, venture capital, and management consulting firm focused on healthcare and technology companies. Prior to Forest Street Capital/SAE Ventures, he was vice president and chief financial officer of Emisphere Technologies, Inc. Mr. Steinhart's other experience includes seven years at CW Group, Inc., a venture capital firm focused on medical technology and biopharmaceutical companies, where he was a general partner and chief financial officer. Mr. Steinhart began his career at Price Waterhouse, now known as PricewaterhouseCoopers. He holds BBA and MBA degrees from Pace University and is a Certified Public Accountant (inactive).

That Mr. Steinhart brings more than 30 years of financial experience to our Board, having served in various executive-level financial positions over the course of his career, and that Mr. Steinhart is a certified public accountant, led us to conclude that Mr. Steinhart should serve as a director and chair the Audit Committee.

Corporate Governance

Our Board of Directors oversees our business affairs and monitors the performance of management. In accordance with our corporate governance principles, our Board of Directors does not involve itself in day-to-day operations. The Directors keep themselves informed through discussions with the Chairman and Chief Executive Officer and other key executives and by reading the reports and other materials that we send them and by participating in Board of Directors and committee meetings.

Term of Office

Our directors are divided into three classes, designated Class I, Class II and Class III. Class I shall consists of two directors, Class II shall consist of one director, and Class III consists of one director. The term of office for each Class I director expires at 2023 Annual Meeting of Stockholders; the term of office for each Class II director expires at the 2024 annual meeting of stockholders; and the term of office for each Class III director expires at the 2022 annual meeting of stockholders.

The term of each director is set forth below or until their successors are duly elected:

Director	Class	Term (from 2021 Annual Meeting)
David Nicholson	Class I	2 years
Richard Steinhart	Class I	2 years
Sandesh Seth	Class II	3 years
Jeffrey W. Chell	Class II	3 years
Ajit Shetty	Class III	1 year

Notwithstanding the foregoing, each director shall serve until his successor is duly elected and qualified, or until his retirement, death, resignation or removal.

Director Independence

We use the definition of "independence" of the NYSE American stock exchange to make this determination. We are listed on the NYSE American under the symbol "ATNM". NYSE MKT corporate governance rule Sec. 803(A)(2) provides that an "independent director" means a person other than an executive officer or employee of the company. No director qualifies as independent unless the issuer's board of directors affirmatively determines that the director does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. Under the NYSE American director independence rules, Jeffrey W. Chell, David Nicholson, Ajit S. Shetty, and Richard I. Steinhart are independent directors of the Company.

Chief Executive Officer Compensation

On August 12, 2020, we and Mr. Seth entered into an employment agreement whereby Mr. Seth will serve as Chairman and Chief Executive Officer until February 24, 2024, unless terminated earlier as set forth in the employment agreement.

Under the terms of the employment agreement, Mr. Seth is entitled to (i) a base salary, which will be determined by the Board and adjusted to be competitively aligned to a range between the 25th and 75th percentile of the relevant market data of chief executive officer positions of similarly situated publicly companies, (ii) a performance bonus with a target of 50% of his annual base salary as well as other multipliers as determined by the Board and (iii) options to purchase shares of common stock of the Company as the Board may grant. For 2020, Mr. Seth's annual base salary was set at $578,191, and for 2021, his annual base salary was set at $615,000.

When and if granted, options will have an exercise price equal to the closing price of the Company's common stock on the date of the approval, and 2% of the grant will vest each month from the grant date until fully vested, in accordance with the 2013 Stock Plan and 2019 Plan. The options will expire 10 years from the grant date, subject to Mr. Seth's continuing service with the Company. Mr. Seth also receives the standard benefits available to other similarly situated employees.

If Mr. Seth's employment as Chief Executive Officer or Chairman is terminated due to death or disability, Mr. Seth will be entitled to earned, but unpaid, salary, benefits and the Pro-Rated Bonus (as defined herein) for the year of termination. Upon termination of his employment for Cause (as defined in the employment agreement), or his resignation without Good Reason (as defined in the employment agreement), Mr. Seth will receive any accrued and unpaid base salary, the Pro-Rated Bonus and benefits through the date of termination.

If we terminate Mr. Seth's employment without Cause, or if Mr. Seth resigns for Good Reason, Mr. Seth will be entitled to (i) a single lump sum payment equal to the 24 months of his compensation, (ii) continued health benefits for 24 months, (iii) immediate vesting of all outstanding equity awards granted to Mr. Seth, and (iv) a single lump sum payment equal to his annual bonus subject to the achievement of the applicable goals, pro-rated based on the number of days in the Company's fiscal year through the date of termination (the "Pro-Rated Bonus").

In addition, if we terminate Mr. Seth's employment without Cause or if Mr. Seth resigns for Good Reason, or if we fail to renew his position as Chief Executive Officer and Chairman on February 21, 2024, in any case, within the 12-month period beginning on the date of a Change in Control (as defined in the 2013 Stock Plan and 2019 Plan), Mr. Seth will be entitled to (i) a single lump sum payment equal to 30 months of his compensation, (ii) continued health benefits for 30 months, (iii) immediate vesting of all outstanding equity awards granted to Mr. Seth, and (iv) a single lump sum payment equal to the Pro-Rated Bonus.

Chief Financial Officer/Principal Financial Officer Compensation

On August 12, 2020, we entered into an employment agreement with Mr. O'Loughlin, pursuant to which he serves as Chief Financial Officer of the Company. Under the terms of the employment agreement, Mr. O'Loughlin is entitled to (i) a base salary, which shall be determined by the Board, (ii) a performance bonus, which may be up to 30% of the annual base salary based upon the achievement of certain objectives such as the Board shall determine and (iii) options to purchase shares of common stock of the Company as the Board may grant. For 2020, Mr. O'Loughlin's annual base salary was set at $330,000, and for 2021, his annual base salary was set at $370,000.

When and if granted, options will have an exercise price equal to the closing price of the Company's common stock on the date of the approval, and 2% of the grant will vest each month from the grant date until fully vested, in accordance with the 2013 Stock Plan and 2019 Plan. The options will expire 10 years from the grant date, subject to Mr. O'Loughlin's continuing service with the Company. Mr. Loughlin will also receive the standard benefits available to other similarly situated employees.

In addition, if we terminate Mr. O'Loughlin's employment without Cause (as defined in the employment agreement) or if Mr. O'Loughlin resigns for Good Reason (as defined in the employment agreement), in either case, within the 12-month period beginning on the date of a Change in Control, Mr. O'Loughlin will be entitled to (i) a single lump sum payment equal to his annual base salary, (ii) continued health benefits for 12 months, and (iii) immediate vesting of all outstanding equity awards granted to Mr. O'Loughlin.

Board of Directors Meetings and Attendance

During 2021, our Board of Directors held fourteen meetings and did not act by unanimous written consent. Each director attended all of the meetings of our Board and of any committees of which he was a member during the year ended December 31, 2021.

Committees of the Board of Directors

Our Board of Directors has formed three standing committees: Audit, Compensation and Nominating and Corporate Governance. Actions taken by our committees are reported to the full board. Each of our committees has a charter and each charter is posted on our website.

Audit Committee	Compensation Committee	Nominating and Corporate Governance Committee
Richard I. Steinhart*	David Nicholson*	Ajit S. Shetty*
Jeffrey W. Chell	Jeffrey W. Chell	David Nicholson
Ajit S. Shetty	Ajit S. Shetty	Richard I. Steinhart

* Indicates committee chair

Audit Committee

Our Audit Committee, which currently consists of three directors, provides assistance to our Board in fulfilling its legal and fiduciary obligations with respect to matters involving the accounting, financial reporting, internal control and compliance functions of the Company. The Board has determined that Mr. Steinhart is an "audit committee financial expert" as defined in Item 407(d)(5)(ii) of Regulation S-K. Our Audit Committee employs an independent registered public accounting firm to audit the financial statements of the Company and perform other assigned duties. Further, our Audit Committee provides general oversight with respect to the accounting principles employed in financial reporting and the adequacy of our internal controls. In discharging its responsibilities, our Audit Committee may rely on the reports, findings and representations of the Company's auditors, legal counsel, and responsible officers. Our Board has determined that all members of the Audit Committee are financially literate within the meaning of SEC rules and under the current listing standards of the NYSE American. The Audit Committee met four times during 2021. Each member of the Audit Committee was present at all of the Audit Committee meetings held during 2021.

Compensation Committee

Our Compensation Committee, which currently consists of three directors, establishes executive compensation policies consistent with the Company's objectives and stockholder interests. The Compensation Committee met one time during 2021. Each member of the Compensation Committee was present at the meeting held in 2021. Our Compensation Committee also reviews the performance of our executive officers and establishes, adjusts and awards compensation, including incentive-based compensation, as more fully discussed below. In addition, our Compensation Committee generally is responsible for:

- establishing and periodically reviewing our compensation philosophy and the adequacy of compensation plans and programs for our directors, executive officers and other employees;
- overseeing our compensation plans, including the establishment of performance goals under the Company's incentive compensation arrangements and the review of performance against those goals in determining incentive award payouts;
- overseeing our executive employment contracts, special retirement benefits, severance, change in control arrangements and/or similar plans;
- acting as administrator of any company stock option plans; and
- overseeing outside compensation consultants when engaged.

Our Compensation Committee periodically reviews the compensation paid to our non-employee directors and the principles upon which their compensation is determined. The Compensation Committee also periodically reports to the Board on how our non-employee director compensation practices compare with those of other similarly situated public corporations and, if the Compensation Committee deems it appropriate, recommends changes to our director compensation practices to our Board for approval.

Outside consulting firms retained by our compensation committee and management also will, if requested, provide assistance to the Compensation Committee in making its compensation-related decisions. We paid consultant fees to StreeterWyatt of $22,000 during the year ended December 31, 2021.

Nominating and Corporate Governance Committee

Our Nominating and Corporate Governance Committee, which currently consists of three directors is charged with the responsibility of reviewing our corporate governance policies and proposing potential director nominees to the Board for consideration. The Nominating and Corporate Governance Committee was formed on November 4, 2021 and met one time during 2021.

Our Nominating and Corporate Governance Committee's primary responsibilities and obligations include, among other things:

- overseeing the administration of our Code of Business Ethics and Conduct and related policies;
- leading the search for and recommending individuals qualified to become members of the Board, and selecting director nominees to be presented for election by the shareholders at each annual meeting;
- ensuring, in cooperation with the Compensation Committee, that no agreements or arrangements are made with directors or relatives of directors for providing professional or consulting services to us or our affiliate or individual officer or one of their affiliated, without appropriate review and evaluation for conflicts of interest;
- assessing the independence of directors annually and report to the Board;
- recommending to the Board for its approval, the leadership structure of the Board, including whether the Board should have an executive or non-executive Chairman, whether the roles of Chairman and Chief Executive Officer should be combined, and whether a Lead Director of the Board should be appointed; provided that such structure shall be subject to the bylaws of the Company then in effect;
- ensuring that Board members do not serve on more than six other for-profit public company boards that have a class of securities registered under the Exchange Act in addition to the Board;
- reviewing the Board's committee structure and to recommend to the Board for its approval directors to serve as members of each committee as well as recommendations for committee chairs;
- reviewing and recommending changes to procedures whereby shareholders may communicate with the Board;
- reviewing recommendations received from shareholders for persons to be considered for nomination to the Board;
- monitoring compliance with our corporate governance guidelines;
- developing and implementing an annual self-evaluation of the Board, both individually and as a Board, and of its committees;

Our Amended and Restated Bylaws, as amended (the "Bylaws") contains provisions that address the process by which a stockholder may nominate an individual to stand for election to the Board at our annual meetings. To recommend a nominee for election to the Board, a stockholder must submit his or her recommendation to our Secretary at our corporate offices at 275 Madison Avenue, 7th Floor, New York, New York 10016. Such nomination must satisfy the notice, information and consent requirements set forth in our Bylaws and must be received by us prior to the date set forth under "Submission of Future Stockholder Proposals" below. A stockholder's recommendation must be accompanied by the information with respect to stockholder nominees as specified in our Bylaws, including among other things, the name, age, address and occupation of the recommended person, the proposing stockholder's name and address, the ownership interests of the proposing stockholder and any beneficial owner on whose behalf the nomination is being made (including the number of shares beneficially owned, any hedging, derivative, short or other economic interests and any rights to vote any shares) and any material monetary or other relationships between the recommended person and the proposing stockholder and/or the beneficial owners, if any, on whose behalf the nomination is being made.

Our approach toward Board diversity takes into consideration the overall composition and diversity of the Board and areas of expertise that director nominees may be able to offer, including business experience, knowledge, abilities, customer relationships and appropriate perspectives on environmental, social and governance matters. Generally, we strive to assemble and maintain a Board that brings to us a variety of perspectives and skills derived from business and professional experience as we may deem are in our and our stockholders' best interests. In doing so, we also consider candidates with appropriate non-business backgrounds.

Lead Director

In September 2017, our board of directors created the position of Lead Director. Our board of directors designated David Nicholson, an existing independent director, as our Lead Director. Pursuant to the charter of the Lead Director, the Lead Director shall be an independent, non-employee director designated by our board of directors who shall serve in a lead capacity to coordinate the activities of the other non-employee directors, interface with and advise management, and perform such other duties as are specified in the charter or as our board of directors may determine.

Family Relationships

There are no family relationships among any of our officers or directors.

Involvement in Certain Legal Proceedings

To our knowledge, none of our current directors or executive officers has, during the past ten years:

- been convicted in a criminal proceeding or been subject to a pending criminal proceeding (excluding traffic violations and other minor offenses);

- had any bankruptcy petition filed by or against the business or property of the person, or of any partnership, corporation or business association of which he was a general partner or executive officer, either at the time of the bankruptcy filing or within two years prior to that time;

- been subject to any order, judgment, or decree, not subsequently reversed, suspended or vacated, of any court of competent jurisdiction or federal or state authority, permanently or temporarily enjoining, barring, suspending or otherwise limiting, his involvement in any type of business, securities, futures, commodities, investment, banking, savings and loan, or insurance activities, or to be associated with persons engaged in any such activity;

- been found by a court of competent jurisdiction in a civil action or by the SEC or the Commodity Futures Trading Commission to have violated a federal or state securities or commodities law, and the judgment has not been reversed, suspended, or vacated;

- been the subject of, or a party to, any federal or state judicial or administrative order, judgment, decree, or finding, not subsequently reversed, suspended or vacated (not including any settlement of a civil proceeding among private litigants), relating to an alleged violation of any federal or state securities or commodities law or regulation, any law or regulation respecting financial institutions or insurance companies including, but not limited to, a temporary or permanent injunction, order of disgorgement or restitution, civil money penalty or temporary or permanent cease-and-desist order, or removal or prohibition order, or any law or regulation prohibiting mail or wire fraud or fraud in connection with any business entity; or

- been the subject of, or a party to, any sanction or order, not subsequently reversed, suspended or vacated, of any self-regulatory organization (as defined in Section 3(a)(26) of the Exchange Act), any registered entity (as defined in Section 1(a)(29) of the Commodity Exchange Act), or any equivalent exchange, association, entity or organization that has disciplinary authority over its members or persons associated with a member.

Except as set forth in our discussion below in "Certain Relationships and Related Transactions," none of our directors or executive officers has been involved in any transactions with us or any of our directors, executive officers, affiliates or associates which are required to be disclosed pursuant to the rules and regulations of the SEC.

Code of Ethics

The Company has adopted a code of ethics, a copy of which is attached as Exhibit 14.1 to the Form 8-K filed on January 2, 2013.

Compliance with Section 16 (a) of the Exchange Act

Under Section 16(a) of the Exchange Act, our directors and certain of our officers, and persons holding more than 10 percent of our common stock are required to file forms reporting their beneficial ownership of our common stock and subsequent changes in that ownership with the United States Securities and Exchange Commission.

Based solely upon a review of copies of such forms filed on Forms 3, 4, and 5, and amendments thereto furnished to us, we believe that as of December 31, 2021, our executive officers and directors have complied on a timely basis with all Section 16(a) filing requirements.

Compensation Discussion and Analysis

Our Compensation Committee of our Board of Directors has the responsibility to review, determine and approve the compensation for our executive officers. Further, our Compensation Committee oversees our overall compensation strategy, including compensation policies, plans and programs that cover all employees. At our 2019 Annual Meeting of Stockholders, our Stockholders voted on an advisory basis with respect to our compensation program during 2018 for named executive officers. Of the votes cast (excluding abstentions and broker non-votes), 72.1% were cast in support of the program. In light of this, in reviewing the executive compensation program for 2020 and 2021, our Compensation Committee decided to retain the general overall program design, which ties a significant portion of the executives' pay closely with our performance. In the future, our Compensation Committee will continue to consider the executive compensation program in light of changing circumstances and stockholder feedback.

We currently employ two executive officers, each of whom serves as a "Named Executive Officer" (or NEO) for purposes of SEC reporting: (1) Sandesh Seth, our Chairman and Chief Executive Officer (who we refer to in this Compensation Discussion and Analysis as our CEO) and (2) Steve O'Loughlin, our Chief Financial Officer. Two executive officers, who were formerly NEOs, Mark Berger, our former Chief Medical Officer and Dale Ludwig, our former Chief Scientific and Technology Officer, both resigned from the Company during 2021.

This Compensation Discussion and Analysis sets forth a discussion of the compensation for our NEOs as well as a discussion of our philosophies underlying the compensation for our NEOs and our employees generally.

Objectives of Our Compensation Program

The Compensation Committee's philosophy seeks to align the interests of our stockholders, officers and employees by tying compensation to individual and company performance, both directly in the form of salary or annual cash incentive payments, and indirectly in the form of equity awards. The objectives of our compensation program enhance our ability to:

- attract and retain qualified and talented individuals; and
- provide reasonable and appropriate incentives and rewards to our team for building long-term value within our company, in each case in a manner comparable to companies similar to ours.

In addition, we strive to be competitive with other similarly situated companies in our industry. The process of developing pharmaceutical products and bringing those products to market is a long-term proposition and outcomes may not be measurable for several years. Therefore, in order to build long-term value for our company and its stockholders, and in order to achieve our business objectives, we believe that we must compensate our officers and employees in a competitive and fair manner that reflects current company activities but also reflects contributions to building long-term value.

We utilize the services of StreeterWyatt Governance LLC to review compensation programs of peer companies in order to assist the Compensation Committee in determining the compensation levels for our NEOs, as well as for other employees of our company. StreeterWyatt is a recognized independent consulting company and services clients throughout the United States.

Elements of Our Compensation Program and Why We Chose Each

Main Compensation Components

Our company-wide compensation program, including for our NEOs, is broken down into three main components: base salary, performance cash bonuses and potential long-term compensation in the form of stock options or restricted stock awards. We believe these three components constitute the minimum essential elements of a competitive compensation package in our industry.

Salary

Base salary is used to recognize the experience, skills, knowledge and responsibilities required of our NEOs as well as recognizing the competitive nature of the biopharmaceutical industry. This is determined partially by evaluating our peer companies as well as the degree of responsibility and experience levels of our NEOs and their overall contributions to our company. Base salary is one component of the compensation package for NEOs; the other components being cash bonuses, annual equity grants, and company benefit programs. Base salary is determined in advance whereas the other components of compensation are awarded in varying degrees following an assessment of the performance of a NEO. This approach to compensation reflects the philosophy of our board of directors and its Compensation Committee to emphasize and reward, on an annual basis, performance levels achieved by our NEOs.

Performance Bonus Plan

We have a performance bonus plan under which bonuses are paid to our NEOs based on achievement of company performance goals and objectives established by the Compensation Committee and/or our board of directors as well as on individual performance. The bonus program is discretionary and is intended to: (i) strengthen the connection between individual compensation and our company's achievements; (ii) encourage teamwork among all disciplines within our company; (iii) reinforce our pay-for-performance philosophy by awarding higher bonuses to higher performing employees; and (iv) help ensure that our cash compensation is competitive. Depending on the cash position of the company, the Compensation Committee and our board of directors have the discretion to not pay cash bonuses in order that we may conserve cash and support ongoing development programs and commercialization efforts. Regardless of our cash position, we consistently grant annual merit-based stock options to continue incentivizing both our senior management and our employees.

Based on their employment agreements, each NEO is assigned a target payout under the performance bonus plan, expressed as a percentage of base salary for the year. Actual payouts under the performance bonus plan are based on the achievement of corporate performance goals and an assessment of individual performance, each of which is separately weighted as a component of such officer's target payout. For the NEOs, the corporate goals receive the highest weighting in order to ensure that the bonus system for our management team is closely tied to our corporate performance. Each employee also has specific individual goals and objectives as well that are tied to the overall corporate goals. For employees, mid-year and end-of-year progress is reviewed with the employees' managers.

Equity Incentive Compensation

We view long-term compensation, currently in the form of stock options generally vesting in annual increments over four years, as a tool to align the interests of our NEOs and employees generally with the creation of stockholder value, to motivate our employees to achieve and exceed corporate and individual objectives and to encourage them to remain employed by the company. While cash compensation is a significant component of employees' overall compensation, the Compensation Committee and our board of directors (as well as our NEOs) believe that the driving force of any employee working in a small biotechnology company should be strong equity participation. We believe that this not only creates the potential for substantial longer-term corporate value but also serves to motivate employees and retain their loyalty and commitment with appropriate personal compensation.

Other Compensation

In addition to the main components of compensation outlined above, we also have provided contractual severance and/or change in control benefits to several employees including our CEO. The change in control benefits for all applicable persons have a "double trigger." A double-trigger means that the executive officers will receive the change in control benefits described in the agreements only if there is both (1) a Change in Control of our company (as defined in the agreements) and (2) a termination by us of the applicable person's employment "without cause" or a resignation by the applicable persons for "good reason" (as defined in the agreements) within a specified time period prior to or following the Change in Control. We believe this double trigger requirement creates the potential to maximize stockholder value because it prevents an unintended windfall to management as no benefits are triggered solely in the event of a Change in Control while providing appropriate incentives to act in furtherance of a change in control that may be in the best interests of the stockholders. We believe these severances or change in control benefits are important elements of our compensation program that assist us in retaining talented individuals at the executive and senior managerial levels and that these arrangements help to promote stability and continuity of our executives and senior management team. Further, we believe that the interests of our stockholders will be best served if the interests of these members of our management are aligned with theirs. We believe that providing change in control benefits lessens or eliminates any potential reluctance of members of our management to pursue potential change in control transactions that may be in the best interests of the stockholders. We also believe that it is important to provide severance benefits to members of our management, to promote stability and focus on the job at hand.

We also provide benefits to the executive officers that are generally available to all regular full-time employees of our company, including our medical and dental insurance, and a 401(k) plan. Further, we do not have deferred compensation plans, pension arrangements or post-retirement health coverage for our executive officers or employees. All of our employees not specifically under contract are "at-will" employees, which means that their employment can be terminated at any time for any reason by either us or the employee.

Determination of Compensation Amounts

A number of factors impact the determination of compensation amounts for our NEOs, including the individual's role in the company and individual performance, length of service with the company, competition for talent, individual compensation package, assessments of internal pay equity and industry data. Stock price performance has generally not been a factor in determining annual compensation because the price of our common stock is subject to a variety of factors outside of our control.

Industry Survey Data

In collaboration with StreeterWyatt, we establish and maintain a list of peer companies to best assure ourselves that we are compensating our executives on a fair and reasonable basis, as set forth above under the heading "Objectives of our Compensation Program." We also utilize StreeterWyatt-prepared data for below-executive level personnel, which data focuses on biotechnology companies that can be considered peers in terms of numerous variables including phase of development, size, therapeutic and technological focus among others. The availability of peer data is used by the Compensation Committee strictly as a guide in determining compensation levels with regard to salaries, cash bonuses and performance related annual equity grants to all employees. However, the availability of this data does not imply that the Compensation Committee is under any obligation to exactly follow peer companies in compensation matters.

Determination of Base Salaries

As a guideline for NEO base salary, we perform formal benchmarks against respective comparable positions in our established peer group. We adjust salaries based on our assessment of our NEOs' levels of responsibility, experience, overall compensation structure and individual performance. The Compensation Committee is not obliged to raise salaries purely on the availability of data. Merit-based increases to salaries of executive officers are based on our assessment of individual performance and the relationship to applicable salary ranges. Cost of living adjustments may also be a part of that assessment.

Performance Bonus Plan

Concurrently with the beginning of each calendar year, preliminary corporate goals that reflect our business priorities for the coming year are prepared by the CEO with input from the other executive officers. These goals are weighted by relative importance. The draft goals and proposed weightings are presented to the Compensation Committee and the Board and discussed, revised as necessary, and then approved by our board of directors. The Compensation Committee then reviews the final goals and their weightings to determine and confirm their appropriateness for use as performance measurements for purposes of the bonus program. The goals and/or weightings may be re-visited during the year and potentially restated in the event of significant changes in corporate strategy or the occurrence of significant corporate events. Following the agreement of our Board on the corporate objectives, the goals are then shared with all employees in formal meetings and are reviewed periodically throughout the year.

Determination of Equity Incentive Compensation

To assist us in assessing the reasonableness of our equity grant amounts, we have reviewed StreeterWyatt supplied information. Such information included equity data from a cross-section of similar companies in our industry.

Equity Grant Practices

All stock options and/or restricted stock granted to the NEOs and other executives are approved by the Compensation Committee. Exercise prices for options are set at the closing price of our common stock on the date of grant. Grants are generally made: (i) on the employee's start date and (ii) at board of director meetings held once each year and following annual performance reviews. However, grants have been made at other times during the year. The size of year-end grants for each NEO is assessed against our internal equity guidelines. Current market conditions for grants for comparable positions and internal equity may also be assessed. Also, grants may be made in connection with promotions or job-related changes in responsibilities. In addition, on occasion, the Compensation Committee may make additional special awards for extraordinary individual or company performance.

Compensation Setting Process

Annually, at a meeting of our Board of Directors and the Compensation Committee, overall corporate performance and relative achievement of the corporate goals for the prior year are assessed. The relative achievement of each goal is assessed and quantified and the summation of the individual components results in a corporate goal rating, expressed as percentages. The Compensation Committee then approves the final disbursement of salary increases, cash bonuses and option or restricted stock grants.

The Compensation Committee looks to the CEO's performance assessments of the other NEOs and his recommendations regarding a performance rating for each, as well as input from the other members of our board of directors. These recommendations may be adjusted by the Compensation Committee prior to finalization. For the CEO, the Compensation Committee evaluates his performance, taking into consideration input from the other members of our board of directors, and considers the achievement of overall corporate objectives by both the CEO specifically and the company generally. The CEO is not present during the Compensation Committee's deliberations regarding his compensation.

The Compensation Committee has the authority to directly engage, at our company's expense, any compensation consultants or other advisors (such as StreeterWyatt) that it deems necessary to determine the amount and form of employee, executive and director compensation. In determining the amount and form of employee, executive and director compensation, the Compensation Committee has reviewed and discussed historical salary information as well as salaries for similar positions at comparable companies. However, the availability of this data does not imply that the Compensation Committee is under any obligation to exactly follow peer companies' compensation practices.

We paid consultant fees to StreeterWyatt of $22,000 during the year ended December 31, 2021. NEOs may have indirect input in the compensation results for other executive officers by virtue of their participation in the performance review and feedback process for the other executive officers.

ITEM 11. EXECUTIVE COMPENSATION

Summary Compensation Table

The following table provides information regarding the compensation earned during the years ended December 31, 2021 and 2020 for our named executive officers.

Name/Position	Year	Salary	Bonus (1)	Option Awards (2)	All Other Compensation	Total
Sandesh Seth	2021	$ 615,000	$ 430,000	$ 1,290,323	$ -	$ 2,335,323
Chairman and Chief Executive Officer	2020	$ 578,191	$ 315,000	$ 938,537	$ -	$ 1,831,728
Mark Berger (3)	2021	$ 304,962	$ -	$ 279,395	$ -	$ 584,357
Former Chief Medical Officer	2020	$ 415,000	$ 100,000	$ 314,958	$ -	$ 829,958
Dale Ludwig (4)	2021	$ 213,068	$ -	$ -	$ -	$ 213,068
Former Chief Scientific and Technology Officer	2020	$ 375,000	$ 105,000	$ 337,453	$ -	$ 817,453
Steve O'Loughlin	2021	$ 370,000	$ 150,000	$ 447,034	$ -	$ 967,034
Chief Financial Officer	2020	$ 330,000	$ 90,000	$ 398,640	$ -	$ 818,640

(1) The bonus disclosed in this column relates to performance in the prior year, but was contingent upon board approval, and was paid in the year disclosed.

(2) The dollar amounts in this column represent the aggregate grant date fair value of all option awards granted during the indicated year. These amounts have been calculated in accordance with FASB ASC Topic 718, using the Black-Scholes option-pricing model. For a discussion of valuation assumptions, see Note 6 to our financial statements. These amounts do not necessarily correspond to the actual value that may be recognized from the option awards by the NEOs.

(3) On September 24, 2021, Dr. Berger resigned as the Chief Medical Officer

(4) On July 26, 2021, Dr. Ludwig resigned as the Chief Scientific and Technology Officer

Narrative Disclosure to Summary Compensation Table

For a discussion of the material terms of each named executive officer's employment agreement or arrangement, refer to the sections above titled "Directors, Executive Officers and Corporate Governance—Chief Executive Officer Compensation" and "Directors, Executive Officers and Corporate Governance—Chief Financial Officer/Principal Financial Officer Compensation."

On September 1, 2021, Mr. Seth was granted an option to purchase 310,182 shares of common stock and Mr. O'Loughlin was granted an option to purchase 107,463 shares of common stock. The options have an exercise price of $6.07 per share and will expire on September 1, 2031. Pursuant to the terms of the Company's Amended and Restated 2019 Stock Plan, 2% of the options will vest each month from September 1, 2021 until fully vested.

Director Compensation

The following table sets forth the compensation of our non-employee directors for the year ended December 31, 2021:

Name	Fees Earned	Stock Awards	Option Awards (1)(2)	All Other Compensation	Total
Jeffrey W. Chell	$ 51,000	-	$ 76,338	-	$ 127,338
David Nicholson	$ 63,000	-	$ 76,338	-	$ 139,338
Ajit J. Shetty	$ 58,500	-	$ 76,338	-	$ 134,838
Richard Steinhart	$ 63,000	-	$ 76,338	-	$ 139,338

(1) The dollar amounts in this column represent the aggregate grant date fair value of all option awards granted during the indicated year. These amounts have been calculated in accordance with FASB ASC Topic 718, using the Black-Scholes option-pricing model. For a discussion of valuation assumptions, see Note 6 to our financial statements. These amounts do not necessarily correspond to the actual value that may be recognized from the option awards by the NEOs.

(2) At December 31, 2021, the aggregate number of option awards outstanding for each director was as follows: (i) for Dr. Chell, 40,017, (ii) for Dr. Nicholson, 46,679, (iii) for Dr. Shetty, 40,017, and (iv) for Mr. Steinhart, 45,015.

Our non-employee directors are paid an annual fee of $40,000 and receive annual option grants. Dr. Nicholson as Lead Director receives an additional annual fee of $10,000. Board committee members receive the following compensation:

BOD Committee	Chairman	Member
Audit	$ 20,000	$ 6,000
Compensation	$ 10,000	$ 5,000
Nominating and Corporate Governance	$ 7,500	$ 3,000

OUTSTANDING EQUITY AWARDS AT FISCAL YEAR-END - 2021

The following table sets forth all unexercised options that have been awarded to our named executives by the Company that were outstanding as of December 31, 2021.

	Option Awards					Stock Awards			
Name (a)	Number of Securities Underlying Unexercised Options (#) (Exercisable) (b)	Number of Securities Underlying Unexercised Options (#) (Unexercisable) (c)	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#) (d)	Option Exercise Price ($) (e)	Option Expiration Date (f)	Number of Shares or Units of Stock That Have Not Vested (#) (g)	Market Value of Shares or Units of Stock That Have Not Vested ($) (h)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#) (i)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($) (j)
Sandesh Seth	832(1)	-	-	45.05	8/30/2022	-	-	-	-
	832(1)	-	-	45.05	12/19/2022	-	-	-	-
	9,333(1)	-	-	183.90	9/23/2024	-	-	-	-
	5,000(1)	-	-	107.40	2/15/2025	-	-	-	-
	16,666(1)	-	-	59.70	4/15/2026	-	-	-	-
	24,998(1)	-	-	41.70	3/14/2027	-	-	-	-
	27,333(2)	6,000	-	23.487	7/13/2028	-	-	-	-
	29,000(2)	21,000	-	6.96	7/12/2029	-	-	-	-
	44,496(2)	94,566	-	9.55	8/12/2030	-	-	-	-
	18,610(2)	291,572	-	6.07	9/01/2031	-	-	-	-
Steve O'Loughlin	3,333(1)	-	-	53.70	9/28/2025	-	-	-	-
	1,666(1)	-	-	59.70	4/15/2026	-	-	-	-
	3,333(1)	-	-	41.70	3/14/2027	-	-	-	-
	7,243(2)	1,590	-	23.487	7/13/2028	-	-	-	-
	7,733(2)	5,600	-	6.96	7/12/2029	-	-	-	-
	18,896(2)	40,170	-	9.55	8/12/2030	-	-	-	-
	6,447(2)	101,016	-	6.07	9/01/2031	-	-	-	-

(1) Fully vested.

(2) Pursuant to the terms of the Company's 2013 Stock Plan, 2% of these options vest each month from the date of grant.

Indemnification of Directors and Officers

Section 102(b)(7) of the Delaware General Corporation Law allows a corporation to provide in its certificate of incorporation that a director of the corporation will not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except where the directors breached the duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides for this limitation of liability.

Section 145 of the General Corporation Law of the State of Delaware provides that a Delaware corporation may indemnify any person who was, is or is threatened to be made, party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of such corporation), by reason of the fact that such person is or was an officer, director, employee or agent of such corporation or is or was serving at the request of such corporation as a director, officer employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, provided such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the corporation's best interests and, with respect to any criminal action or proceeding, had no reasonable cause to believe that his conduct was illegal. A Delaware corporation may indemnify any persons who are, or were, a party to any threatened, pending or completed action or suit by or in the right of the corporation by reason of the fact that such person is or was a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit, provided such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the corporation's best interests, provided that no indemnification is permitted without judicial approval if the officer, director, employee or agent is adjudged to be liable to the corporation. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, the corporation must indemnify him against the expenses which such officer or directors has actually and reasonably incurred.

Section 145 further authorizes a corporation to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation or enterprise, against any liability asserted against him and incurred by him in any such capacity, or arising out of his status as such, whether or not the corporation would otherwise have the power to indemnify him under Section 145.

Our bylaws provide that we will indemnify our directors and officers to the fullest extent authorized by the General Corporation Law of the State of Delaware. Expenses (including attorneys' fees) incurred by an officer or director of the Corporation in defending any civil, criminal, administrative or investigative action, suit or proceeding may be paid by the Company in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of such director or officer to repay such amount if it shall ultimately be determined that such person is not entitled to be indemnified by the Company as authorized under Delaware law. Such expenses (including attorneys' fees) incurred by former directors and officers or other employees and agents of the Company or by persons serving at the request of the Company as directors, officers, employees or agents of another corporation, partnership, joint venture, trust or other enterprise may be so paid upon such terms and conditions, if any, as the Company deems appropriate.

The indemnification rights set forth above shall not be exclusive of any other right which an indemnified person may have or hereafter acquire under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in such person's official capacity and as to action in another capacity while holding such office, and shall continue as to a person who has ceased to be a director, officer, employee, or agent and shall inure to the benefit of the heirs, executors, and administrators of such person.

We maintain a general liability insurance policy that covers liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers. We have also entered into Indemnification Agreements with our executive officers and directors.

At the present time, there is no pending litigation or proceeding involving a director, officer, employee, or other agent of ours in which indemnification would be required or permitted. We are not aware of any threatened litigation or proceeding that may result in a claim for such indemnification.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table shows the beneficial ownership of our Common Stock as of March 25, 2022 held by (i) each person known to us to be the beneficial owner of more than five percent (5%) of any class of our shares; (ii) each director; (iii) each executive officer; and (iv) all directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the SEC, and generally includes voting power and/or investment power with respect to the securities held. Shares of Common Stock subject to options and warrants currently exercisable or which may become exercisable within 60 days of March 25, 2022, are deemed outstanding and beneficially owned by the person holding such options or warrants for purposes of computing the number of shares and percentage beneficially owned by such person, but are not deemed outstanding for purposes of computing the percentage beneficially owned by any other person. Except as indicated in the footnotes to this table, the persons or entities named have sole voting and investment power with respect to all shares of our Common Stock shown as beneficially owned by them.

Unless otherwise indicated, the principal address of each of the persons below is c/o Actinium Pharmaceuticals, Inc., 275 Madison Ave, 7th floor, New York, NY 10016.

Name of Beneficial Owner	Number of Shares of Common Stock Beneficially Owned	Percentage of Ownership[(a)]
Beneficial Owners of 5% or More of Our Common Stock		
Michael Bigger	1,314,106(1)	5.9%
Name Executive Officers and Directors		
Sandesh Seth	235,738(2)	1.0%
Steve O'Loughlin	68,702(3)	*
Jeffrey W. Chell, M.D.	16,888(4)	*
David Nicholson, Ph.D.	23,883(5)	*
Ajit S. Shetty, Ph.D.	17,645(6)	*
Richard I. Steinhart	22,182(7)	*
All Directors and Officers as a Group (6 persons)	385,038(8)	1.7%

* less than 1%

(a) Based on 22,143,974 shares of common stock outstanding as of March 25, 2022

(1) The address of record is 2250 Red Springs Drive, Las Vegas, NV 89135. Based on the beneficial owner's Schedule 13G filed February 9, 2022, shares beneficially owned consist of 323,236 shares of Common Stock owned by Bigger Capital Fund, LP ("Bigger Capital"), 118,417 shares of Common Stock issuable upon exercise of Warrants owned by Bigger Capital, 513,099 shares of Common Stock owned by District 2 Capital Fund LP ("District 2 CF"), 160,475 shares of Common Stock issuable upon exercise of Warrants owned by District 2 CF, 150,000 shares of Common Stock held by Mr. Bigger through an IRA and another account, 107,771 shares of Common Stock through an IRA held by Patricia Winter, the spouse of Mr. Bigger and an aggregate of 220,000 shares of Common Stock through an IRA held by the sons of Mr. Bigger. The warrants are subject to a 4.99% beneficial ownership limit. The number of shares and percentage set forth above assume the no exercise of the warrants due to the beneficial ownership limit. Mr. Bigger disclaims beneficial ownership of these securities.

(2) Excludes warrants to purchase an aggregate of 12,518 shares of common stock of the Company at par value per share, exercisable on a cashless basis issued to Amrosan, LLC as the warrants are not exercisable upon less than 90 days' notice. The holder may waive the 90-day exercise notice requirement by giving 65 days prior notice of such waiver. Excludes warrants to purchase an aggregate of 11,767 shares of common stock issued to Carnegie Hill Asset Partners and irrevocable trust linked to Mr. Seth's family and warrants to purchase an aggregate of 24,035 shares of common stock issued to Bioche Asset Management, LLC, a partnership in which the majority member interest is owned by the family of Mr. Seth, whose terms are the same as those issued to Amrosan LLC. On August 30, 2012 and December 19, 2012, Mr. Seth was granted options to purchase an aggregate of 1,664 shares of common stock at an exercise price of $45.05 per share. On September 23, 2014, Mr. Seth was granted an option to purchase 9,333 shares of common stock with an exercise price of $183.90 per share. On February 18, 2015, Mr. Seth was granted an option to purchase 5,000 shares of common stock with an exercise price of $107.40 per share. On April 15, 2016, Mr. Seth was granted an option to purchase 16,666 shares of common stock at an exercise price of $59.70 per share. On March 14, 2017, Mr. Seth was granted options to purchase an aggregate of 24,998 shares of common stock at an exercise price of $41.70 per share. On July 13, 2018, Mr. Seth was granted an option to purchase 33,333 shares of common stock at an exercise price of $23.487 per share. On July 12, 2019, Mr. Seth was granted an option to purchase 50,000 shares of common stock at an exercise price of $6.96 per share. On August 12, 2020, Mr. Seth was granted an option to purchase 139,062 shares of common stock at an exercise price of $9.55 per share. On September 1, 2021, Mr. Seth was granted an option to purchase 310,182 shares of common stock at an exercise price of $6.07 per share. All options are subject to vesting. Within 60 days of March 25, 2022, options to purchase an aggregate of 230,357 shares of common stock will have vested. Includes 5,381 shares of common stock.

(3) On October 1, 2015, Mr. O'Loughlin was granted options to purchase 3,333 shares of common stock with an exercise price of $53.70 per share. On April 15, 2016, Mr. O'Loughlin was granted options to purchase of 1,666 shares of common stock at an exercise price of $59.70 per share. On March 14, 2017, Mr. O'Loughlin was granted options to purchase 3,333 shares of common stock at an exercise price of $41.70 per share. On July 13, 2018, Mr. O'Loughlin was granted an option to purchase 8,833 shares of common stock at an exercise price of $23.487 per share. On July 12, 2019, Mr. O'Loughlin was granted an option to purchase 13,333 shares of common stock at an exercise price of $6.96 per share. On August 12, 2020, Mr. O'Loughlin was granted an option to purchase 59,066 shares of common stock at an exercise price of $9.55 per share. On September 1, 2021, Mr. O'Loughlin was granted an option to purchase 107,463 shares of common stock at an exercise price of $6.07 per share. All options are subject to vesting. Within 60 days of March 25, 2022, options to purchase an aggregate of 67,519 shares of common stock will have vested. Includes 1,183 shares of common stock.

(4) On April 27, 2018, Dr. Chell was granted an option to purchase 2,500 shares of common stock with an exercise price of $10.41 per share. On July 13, 2018, Dr. Chell was granted an option to purchase 2,500 shares of common stock at an exercise price of $23.487 per share. On July 12, 2019, Dr. Chell was granted an option to purchase 8,333 shares of common stock at an exercise price of $6.96 per share. On August 12, 2020, Dr. Chell was granted an option to purchase 8,333 shares of common stock at an exercise price of $9.55 per share. On September 1, 2021, Dr. Chell was granted an option to purchase 18,351 shares of common stock at an exercise price of $6.07 per share. All options are subject to vesting. Within 60 days of March 25, 2022, options to purchase an aggregate of 16,888 shares of common stock will have vested.

(5) On February 12, 2012, Dr. Nicholson was granted an option to purchase 1,665 shares of common stock at an exercise price of $23.51 per share and on August 12, 2012 and December 19, 2012, Dr. Nicholson was granted options to purchase an aggregate of 1,664 shares of common stock at an exercise price of $45.05 per share. On February 18, 2015, Dr. Nicholson was granted an option to purchase 833 shares of common stock with an exercise price of $107.40 per share. On April 15, 2016, Dr. Nicholson was granted an option to purchase 2,500 shares of common stock at an exercise price of $59.70 per share. On March 14, 2017, Dr. Nicholson was granted an option to purchase 2,500 shares of common stock at an exercise price of $41.70 per share. On July 13, 2018, Dr. Nicholson was granted an option to purchase 2,500 shares of common stock at an exercise price of $23.487 per share. On July 12, 2019, Dr. Nicholson was granted an option to purchase 8,333 shares of common stock at an exercise price of $6.96 per share. On August 12, 2020, Dr. Nicholson was granted an option to purchase 8,333 shares of common stock at an exercise price of $9.55 per share. On September 1, 2021, Dr. Nicholson was granted an option to purchase 18,351 shares of common stock at an exercise price of $6.07 per share. All options are subject to vesting. Within 60 days of March 25, 2022, options to purchase an aggregate of 23,550 shares of common stock will have vested. Includes 333 shares of common stock.

(6) On March 28, 2017, Dr. Shetty was granted an option to purchase 2,500 shares of common stock with an exercise price of $47.40 per share. On July 13, 2018, Dr. Shetty was granted an option to purchase 2,500 shares of common stock at an exercise price of $23.487 per share. On July 12, 2019, Dr. Shetty was granted an option to purchase 8,333 shares of common stock at an exercise price of $6.96 per share. On August 12, 2020, Dr. Shetty was granted an option to purchase 8,333 shares of common stock at an exercise price of $9.55 per share. On September 1, 2021, Dr. Shetty was granted an option to purchase 18,351 shares of common stock at an exercise price of $6.07 per share. All options are subject to vesting. Within 60 days of March 25, 2022, options to purchase an aggregate of 16,888 shares of common stock will have vested. Includes 757 shares of common stock.

(7) On December 16, 2013 Mr. Steinhart was granted an option to purchase 1,665 shares of common stock at an exercise price of $201.00 per share. On February 18, 2015, Mr. Steinhart was granted an option to purchase 833 shares of common stock at an exercise price of $107.40 per share. On April 15, 2016, Mr. Steinhart was granted an option to purchase 2,500 shares of common stock at an exercise price of $59.70 per share. On March 14, 2017, Mr. Steinhart was granted an option to purchase 2,500 shares of common stock at an exercise price of $41.70 per share. On July 13, 2018, Mr. Steinhart was granted an option to purchase 2,500 shares of common stock at an exercise price of $23.487 per share. On July 12, 2019, Mr. Steinhart was granted an option to purchase 8,333 shares of common stock at an exercise price of $6.96 per share. On August 12, 2020, Mr. Steinhart was granted an option to purchase 8,333 shares of common stock at an exercise price of $9.55 per share. On September 1, 2021, Mr. Steinhart was granted an option to purchase 18,351 shares of common stock at an exercise price of $6.07 per share. All options are subject to vesting. Within 60 days of March 25, 2022, options to purchase an aggregate of 21,866 shares of common stock will have vested. Includes 316 shares of common stock.

(8) Includes vested options to purchase 377,068 shares of common stock and 7,970 shares of common stock.

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

Transactions with Related Persons

None.

Director Independence

For disclosures regarding our policies relating to director independence, refer to the section above titled "Directors, Executive Officers and Corporate Governance—Corporate Governance—Director Independence."

Non-Competition Agreements

Our executive officers have signed non-competition agreements, which provide that all inventions become the immediate property of us and require invention assignments. The agreements provide that the executive officers will hold proprietary information in the strictest confidence and not use the confidential information for any purpose not expressly authorized by us.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The table below shows the aggregate fees billed for professional services for the audits and audit-related fees of the Company's annual financial statements included in Form 10-K for the years ending December 31, 2021 and 2020, respectively, by Marcum LLP (PCAOB ID Number 688).

	Year Ended December 31, 2021	Year Ended December 31, 2020
Audit Fees	$ 128,400	$ 130,004
Audit – Related Fees	20,600	83,630
Tax Fees	-	-
All Other Fees	-	-
Total	$ 149,000	$ 213,634

Audit Fees. This category includes the audit of our annual consolidated financial statements, reviews of our financial statements included in our Form 10-Qs and services that are normally provided by our independent registered public accounting firm in connection with its engagements for those years.

Audit-Related Fees. This category consists of assurance and related services by our independent registered public accounting firm that are reasonably related to the performance of the audit or review of our financial statements and are not reported above under "Audit Fees." The services for the fees disclosed under this category include consents regarding equity issuances.

Pre-Approval Policy

In 2015, the Audit Committee adopted policies and procedures for the pre-approval of audit and non-audit services performed by the independent registered public accountants pursuant to which the Audit Committee generally is required to pre-approve the audit and permissible non-audit services performed by the independent registered public accountants in order to ensure that the provision of such services does not impair the registered accountants' independence.

All of the services rendered by Marcum in 2021 were pre-approved by the Audit Committee.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

Exhibit Number	Description
1.1	Underwriting Agreement, dated September 28, 2016, by and between H.C. Wainwright & Co., LLC and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 1.1 to Form 8-K filed on September 29, 2016).
1.2	At Market Issuance Sales Agreement, dated March 16, 2017, between FBR Capital Markets & Co, and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 1.2 to Form S-3 filed on March 16, 2017).
1.3	Amended and Restated At-the-Market Market Issuance Sales Agreement, dated July 3, 2017, among FBR Capital Markets & Co., MLV & Co. LLC, JonesTrading Institutional Services LLC, and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.5 to Form 10-Q filed on August 4, 2017).
1.4	Underwriting Agreement, dated as of July 28, 2017, by and between Actinium Pharmaceuticals, Inc. and Oppenheimer & Co. Inc. as representative of the several underwriters party thereto (incorporated by reference to Exhibit 1.1 to Form 8-K filed on July 28, 2017).
1.5	Dealer-Manager Agreement, dated February 15, 2018, between Maxim Group LLC and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 1.1 to Form 8-K filed on February 15, 2018).
1.6	Underwriting Agreement, dated April 18, 2019, by and between Actinium Pharmaceuticals, Inc. and William Blair & Company, LLC (incorporated by reference to Exhibit 1.1 to Form 8-K filed on April 18, 2019).
1.7	Underwriting Agreement, dated as of April 21, 2020, by and between Actinium Pharmaceuticals, Inc. and H.C. Wainwright & Co., LLC. (incorporated by reference to Exhibit 1.1 to Form 8-K filed on April 24, 2020).
1.8	Capital on Demand™ Sales Agreement, dated August 7, 2020, by and between Actinium Pharmaceuticals, Inc. and JonesTrading Institutional Services LLC (incorporated by reference to Exhibit 1.2 to Registration Statement on Form S-3 filed on August 7, 2020).
2.1	Share Exchange Agreement, dated December 28, 2012, by and among Cactus Ventures, Inc., Actinium Pharmaceuticals, Inc., Diane S. Button, and the shareholders of Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to Form 8-K filed on January 2, 2013).
2.2	Share Exchange Agreement, dated March 11, 2013, by and among Cactus Ventures, Inc., Actinium Pharmaceuticals, Inc, and the shareholders of Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 to Form 8-K filed on March 11, 2013).
2.3	Share Exchange Agreement, dated August 22, 2013, by and among Actinium Pharmaceuticals, Inc, Actinium Corporation, and the shareholders of Actinium Corporation (incorporated by reference to Exhibit 2.3 to Form S-1/A filed on August 22, 2013).
3.1	Certificate of Incorporation of Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 3.1 of the Company's Form 8-K filed with the SEC on April 17, 2013).
3.2	Certificate of Amendment to Certificate of Incorporation filed January 7, 2014 (incorporated by reference to Exhibit 3.5 to Form S-1 filed on January 31, 2014).
3.3	Certificate of Amendment to Certificate of Incorporation filed February 3, 2014. (incorporated by reference to Exhibit 3.1 to Form 8-K filed on February 7, 2014).
3.4	Certificate of Amendment to Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to Form 8-K filed on March 4, 2015).
3.5	Certificate of Amendment to Actinium's Certificate of Incorporation, as amended, filed on February 26, 2018 (incorporated by reference to Exhibit 3.1 to Form 8-K filed on February 26, 2018).

3.6	Certificate of Amendment to Actinium's Certificate of Incorporation, as amended, filed on March 6, 2019 (incorporated by reference to Exhibit 3.7 to Form 10-K filed on March 15, 2019).
3.7	Certificate of Amendment to Certificate of Incorporation, as amended, filed on June 16, 2020 (incorporated by reference to Exhibit 3.1 to Form 8-K filed on June 16, 2020).
3.8	Amended and Restated Bylaws, dated August 8, 2018 (incorporated by reference to Exhibit 3.1 to Form 10-Q filed on August 9, 2018).
3.9	Amendment to the Amended and Restated Bylaws, dated May 7, 2020 (incorporated by reference to Exhibit 3.1 to Form 8-K filed on May 5, 2020).
4.1	Form of Common Stock Warrant, dated December 27, 2013 and January 10, 2014 (incorporated by reference to Exhibit 4.8 to Form S-1 filed on January 31, 2014).
4.2	Form of Warrant (incorporated by reference to Exhibit 4.1 to Form 8-K filed on February 6, 2015).
4.3	Form of Warrant (incorporated by reference to Exhibit 10.1 to Form 8-K filed on July 28, 2017).
4.4	Form of Warrant Agency Agreement between Action Stock Transfer Corporation and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 4.1 to Form 8-K filed on February 15, 2018).
4.5	Form of Series A Warrant (incorporated by reference to Exhibit 4.2 to Form 8-K filed on February 15, 2018).
4.6	Form of Series B Warrant (incorporated by reference to Exhibit 4.3 to Form 8-K filed on February 15, 2018).
4.7	Form of Non-Transferable Subscription Rights Certificate (incorporated by reference to Exhibit 4.4 to Form 8-K filed on February 15, 2018).
4.8	Revised Form of Non-Transferable Subscription Rights Certificate. (incorporated by reference to Exhibit 4.1 to Form 8-K filed on February 26, 2018).
4.9	Amendment to Warrant to Purchase Common Stock, dated November 8, 2018, issued to Amrosan LLC (incorporated by reference to Exhibit 4.1 to Form 10-Q filed on November 9, 2018).
4.10	Amendment to Warrant to Purchase Common Stock, dated November 8, 2018, issued to Carnegie Hill Partners (incorporated by reference to Exhibit 4.2 to Form 10-Q filed on November 9, 2018).
4.11	Amendment to Warrant to Purchase Common Stock, dated November 8, 2018, issued to Bioche Asset Management, LLC (incorporated by reference to Exhibit 4.3 to Form 10-Q filed on November 9, 2018).
4.12	Form of Warrant (incorporated by reference to Exhibit 4.1 to Form 8-K filed on April 18, 2019).
4.13	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to Form 8-K filed on April 24, 2020).
4.14	Form of Pre-Funded Common Stock Warrant (incorporated by reference to Exhibit 4.1 to Form 8-K filed on June 18, 2020).
4.15	Description of Securities (incorporated by reference to Exhibit 4.15 to Form 10 K filed on March 31, 2021)
10.1#	Third Amendment to the 2013 Amended and Restated Stock Plan, effective as of December 22, 2015 (incorporated by reference to Exhibit 10.56 to Form 10-K filed on March 11, 2016).
10.2	Office Space License Agreement, dated March 19, 2016, by and between Actinium Pharmaceuticals, Inc. and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.57 to Form 10-K filed on March 11, 2016).
10.3#	Fourth Amendment to the 2013 Amended and Restated Stock Plan, effective as of December 13, 2016 (incorporated by reference to Exhibit 1.1 to Form 8-K filed on December 14, 2016).
10.4#	Fifth Amendment to the 2013 Amended and Restated Stock Plan, as amended (incorporated by reference to Exhibit 10.59 to Form 10-K filed on March 16, 2017).
10.5#	Amendment to Employment Agreement, dated March 16, 2017, by and between Actinium Pharmaceuticals, Inc. and Dragan Cicic. (incorporated by reference to Exhibit 10.60 to Form 10-K filed on March 16, 2017).

10.6	Amendment to Actinium Pharmaceuticals, Inc. Warrant to Purchase Common Stock, dated March 14, 2017 issued to Sandesh Seth (incorporated by reference to Exhibit 10.61 to Form 10-K filed on March 16, 2017).
10.7	Amendment to Actinium Pharmaceuticals, Inc. Warrant to Purchase Common Stock, dated March 14, 2017 issued to Amrosan LLC (incorporated by reference to Exhibit 10.62 to Form 10-K filed on March 16, 2017).
10.8	Warrant to Purchase Common Stock of Actinium Pharmaceuticals, Inc., dated March 14, 2017, issued to Sandesh Seth (incorporated by reference to Exhibit 10.63 to Form 10-K filed on March 16, 2017).
10.9#	Offer Letter, dated December 27, 2016, by and between Dr. Mark S. Berger and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.64 to Form 10-K filed on March 16, 2017).
10.10	Confidential Information and Invention Assignment Agreement, dated December 27, 2016, by and between Dr. Mark S. Berger and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.65 to Form 10-K filed on March 16, 2017).
10.11#	Indemnification Agreement, dated March 16, 2017, by and between Actinium Pharmaceuticals, Inc. and Mark S. Berger (incorporated by reference to Exhibit 10.66 to Form 10-K filed on March 16, 2017).
10.12#	Director Agreement, dated March 28, 2017, between Ajit S. Shetty and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 to Form 8-K filed on March 28, 2017).
10.13#	Indemnity Agreement, dated March 28, 2017, between Ajit S. Shetty and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.2 to Form 8-K filed on March 28, 2017).
10.14	Confidential Information and Invention Assignment Agreement, dated March 28, 2017, between Ajit S. Shetty and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.3 to Form 8-K filed on March 28, 2017).
10.15#	Amendment to Amended and Restated Consulting Agreement, dated May 5, 2017, by and between Actinium Pharmaceuticals, Inc. and Sandesh Seth (incorporated by reference to Exhibit 10.1 to Form 8-K filed on May 11, 2017).
10.16#	Offer Letter, dated September 17, 2015, between Steve O'Loughlin and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 to Form 10-Q filed on May 15, 2017).
10.17#	Indemnification Agreement, dated May 15, 2017, between Steve O'Loughlin and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.2 to Form 10-Q filed on May 15, 2017).
10.18	Assignment and Consent Agreement, dated June 6, 2017, between 275 Madison Avenue RPW 1 LLC and 275 Madison Avenue RPW 2 LLC, Relmada Therapeutics, Inc., and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 to Form 10-Q filed on August 4, 2017).
10.19	Amended and Restated License Agreement, Dated June 8, 2017, between Relmada Therapeutics, Inc., and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.3 to Form 10-Q filed on August 4, 2017).
10.20#	Offer Letter, dated May 26, 2017, between Nitya G. Ray and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.4 to Form 10-Q filed on August 4, 2017).
10.21#	Agreement, dated June 6, 2017, between Sergio Traversa and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.6 to Form 10-Q filed on August 4, 2017).
10.22#	Consulting Agreement, dated May 22, 2017, between Dragan Cicic and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.7 to Form 10-Q filed on August 4, 2017).
10.23#	Separation and Settlement Agreement, dated May 12, 2017, between Kaushik Dave and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.8 to Form 10-Q filed on August 4, 2017).
10.24#	Separation and Settlement Agreement, dated May 12, 2017, between Dragan Cicic and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.9 to Form 10-Q filed on August 4, 2017).
10.25#	Sixth Amendment to the 2013 Amended and Restated Stock Plan, as amended (incorporated by reference to Exhibit 10.56 to Form 10-K filed on March 16, 2018).

10.26#	Offer Letter, effective January 2, 2018, between Dale L. Ludwig and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.57 to Form 10-K filed on March 16, 2018).
10.27#	Indemnification Agreement, dated January 5, 2018, between Dale L. Ludwig and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.58 to Form 10-K filed on March 16, 2018).
10.28#	Offer Letter, effective January 31, 2018, between Anil Kapur and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.59 to Form 10-K filed on March 16, 2018).
10.29#	Indemnification Agreement, dated February 8, 2018, between Anil Kapur and Actinium Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.60 to Form 10-K filed on March 16, 2018).
10.30#	Director Agreement, dated April 27, 2018, by and between Actinium Pharmaceuticals, Inc. and Jeffrey W. Chell (incorporated by reference to Exhibit 10.1 to Form 8-K filed on May 1, 2018).
10.31#	Indemnity Agreement, dated April 27, 2018, by and between Actinium Pharmaceuticals, Inc. and Jeffrey W. Chell (incorporated by reference to Exhibit 10.2 to Form 8-K filed on May 1, 2018).
10.32	Confidential Information and Invention Assignment Agreement, dated April 27, 2018, by and between Actinium Pharmaceuticals, Inc. and Jeffrey W. Chell (incorporated by reference to Exhibit 10.3 to Form 8-K filed on May 1, 2018).
10.33#	Employment Agreement, dated August 8, 2018, by and between Actinium Pharmaceuticals, Inc. and Sandesh Seth (incorporated by reference to Exhibit 10.1 to Form 10-Q filed on August 9, 2018).
10.34#	Employment Agreement, dated August 8, 2018, by and between Actinium Pharmaceuticals, Inc. and Steve O'Loughlin (incorporated by reference to Exhibit 10.2 to Form 10-Q filed on August 9, 2018).
10.35	Purchase Agreement, dated October 18, 2018, by and between Actinium Pharmaceuticals, Inc. and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 10.1 to Form 8-K filed on October 18, 2018).
10.36	Registration Rights Agreement, dated October 18, 2018, by and between Actinium Pharmaceuticals, Inc. and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 10.2 to Form 8-K filed on October 18, 2018).
10.37#	Consulting Agreement, dated December 21, 2018, between Actinium Pharmaceuticals, Inc. and Nitya Ray (incorporated by reference to Exhibit 10.37 to Form 10-K filed on March 15, 2019).
10.38	Amended and Restated At Market Issuance Sales Agreement, dated December 28, 2018, by and among Actinium Pharmaceuticals, Inc. and B. Riley FBR, Inc. and JonesTrading Institutional Services LLC (incorporated by reference to Exhibit 10.38 to Form 10-K filed on March 15, 2019).
10.39	Seventh Amendment to the 2013 Amended and Restated Stock Plan, as amended (incorporated by reference to Exhibit 10.39 to Form 10-K filed on March 15, 2019).
10.40	Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to Form 8-K filed on June 18, 2020).

10.41#	Amendment to Warrant to Purchase Common Stock of Actinium Pharmaceuticals, Inc., dated August 12, 2017, issued to Sandesh Seth (incorporated by reference to Exhibit 10.2 to Form 10-Q filed on August 14, 2020).
10.42#	Employment Agreement, dated August 12, 2020, by and between Actinium Pharmaceuticals, Inc. and Sandesh Seth (incorporated by reference to Exhibit 10.3 to Form 10-Q filed on August 14, 2020).
10.43#	Employment Agreement, dated August 12, 2020, by and between Actinium Pharmaceuticals, Inc. and Steve O'Loughlin (incorporated by reference to Exhibit 10.4 to Form 10-Q filed on August 14, 2020).
10.44#	Employment Agreement, dated August 12, 2020, by and between Actinium Pharmaceuticals, Inc. and Dale Ludwig (incorporated by reference to Exhibit 10.5 to Form 10-Q filed on August 14, 2020).
10.45#	Employment Agreement, dated August 12, 2020, by and between Actinium Pharmaceuticals, Inc. and Mark Berger (incorporated by reference to Exhibit 10.6 to Form 10-Q filed on August 14, 2020).
10.46#	Actinium Pharmaceuticals, Inc. 2019 Stock Plan (incorporated by reference to Exhibit 10.1 to Form 8-K filed on November 20, 2020).
10.47#	First Amendment to the Actinium Pharmaceuticals, Inc. 2019 Plan (incorporated by reference to Exhibit 10.2 to Form 8-K filed on November 20, 2020).
10.48#	Second Amendment to the Actinium Pharmaceuticals, Inc. 2019 Plan (incorporated by reference to Exhibit 10.1 to Form 8-K filed on November 9, 2021).
14.1	Code of Ethics (incorporated by reference to Exhibit 14.1 to Form 8-K filed on January 2, 2013).
21.1	List of Subsidiaries (incorporated by reference to Exhibit 21.1 to Form 10-K filed on March 16, 2015).
23.1*	Consent of Marcum LLP.
31.1*	Certification of Principal Executive Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial and Accounting Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Principal Financial and Accounting Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS **	Inline XBRL Instance Document
101.SCH **	Inline XBRL Taxonomy Schema Document
101.CAL **	Inline XBRL Taxonomy Calculation Linkbase Document
101.DEF **	Inline XBRL Taxonomy Definition Linkbase Document
101.LAB **	Inline XBRL Taxonomy Label Linkbase Document
101.PRE **	Inline XBRL Taxonomy Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

* Filed herewith.
** Furnished herewith.
# Indicates a management contract or compensatory plan or arrangement.

SIGNATURES

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.

Dated: March 25, 2022

ACTINIUM PHARMACEUTICALS, INC.

By: /s/ Sandesh Seth
Sandesh Seth
Chairman and Chief Executive Officer (Duly Authorized Officer,
Principal Executive Officer)

By: /s/ Steve O'Loughlin
Steve O'Loughlin
Chief Financial Officer
(Duly Authorized Officer,
Principal Financial and Accounting Officer)

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

Signature	Title	Date
/s/ Sandesh Seth Sandesh Seth	Chairman and Chief Executive Officer (Principal Executive Officer)	March 25, 2022
/s/ Jeffrey Chell Jeffrey Chell	Director	March 25, 2022
/s/ David Nicholson David Nicholson	Director	March 25, 2022
/s/ Richard I. Steinhart Richard I. Steinhart	Director	March 25, 2022
/s/ Ajit J. Shetty Ajit J. Shetty	Director	March 25, 2022

Exhibit 23.1

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM'S CONSENT

We consent to the incorporation by reference in the Registration Statement of Actinium Pharmaceuticals, Inc. on Form S-3 (File No. 333-242322) and on Form S-8 (File No. 333-231391, 333-223741, 333-216746, 333-197283), of our report dated March 25, 2022, with respect to our audits of the consolidated financial statements of Actinium Pharmaceuticals, Inc. as of December 31, 2021 and 2020 and for each of the two years in the period ended December 31, 2021, which report is included in this Annual Report on Form 10-K of Actinium Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ Marcum LLP

Marcum LLP
Houston, Texas
March 25, 2022

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO 18U.S.C SECTION 1350 AS ADOPTED
PURSUANT TO SECTION 302 OF THE SARBANES-OXELY ACT OF 2002

I, Sandesh Seth, certify that:

1. I have reviewed this report on Form 10-K of Actinium Pharmaceuticals, Inc. for the fiscal year ended December 31, 2021.

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a–15(e) and 15d–15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a–15(f) and 15d–15(f)) for the registrant and have:

a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 25, 2022

By: /s/ Sandesh Seth
Sandesh Seth
Chairman and Chief Executive Officer
(Duly Authorized Officer,
Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL AND ACCOUNTING OFFICER
PURSUANT TO 18 U.S.C SECTION 1350 AS ADOPTED
PURSUANT TO SECTION 302 OF THE SARBANES-OXELY ACT OF 2002

I, Steve O'Loughlin, certify that:

1. I have reviewed this report on Form 10-K of Actinium Pharmaceuticals, Inc. for the fiscal year ended December 31, 2021.

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a–15(e) and 15d–15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a–15(f) and 15d–15(f)) for the registrant and have:

a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 25, 2022

By: /s/ Steve O'Loughlin
Steve O'Loughlin
Chief Financial Officer
(Duly Authorized Officer,
Principal Financial and Accounting Officer)

Exhibit 32.1

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER,
PURSUANT TO 18 U.S.C. SECTION 1350,AS ADOPTED
PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Actinium Pharmaceuticals, Inc. a Delaware corporation (the “Company”), on Form 10-K for the period ended December 31, 2021 as filed with the Securities and Exchange Commission (the “Report”), I, Sandesh Seth, Chief Executive Officer of the Company, certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350), that to my knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934 (15 U.S.C. 78m or 78o(d)); and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 25, 2022

By: /s/ Sandesh Seth
Sandesh Seth
Chairman and Chief Executive Officer
(Duly Authorized Officer,
Principal Executive Officer)

Exhibit 32.2

CERTIFICATION OF PRINCIPAL FINANCIAL AND ACCOUNTING OFFICER, PURSUANT TO 18 U.S.C. SECTION 1350,AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Actinium Pharmaceuticals, Inc. a Delaware corporation (the “Company”), on Form 10-K for the period ended December 31, 2021 as filed with the Securities and Exchange Commission (the “Report”), I, Steve O’Loughlin, Chief Financial Officer of the Company, certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350), that to my knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934 (15 U.S.C. 78m or 78o(d)); and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 25, 2022

By: /s/ Steve O’Loughlin
Steve O’Loughlin
Chief Financial Officer
(Duly Authorized Officer,
Principal Financial and Accounting Officer)