PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

A. Directors and Senior Management

Not applicable

B. Advisors

Not applicable

C. Auditors

Not applicable

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

You should carefully consider the risks we describe below, in addition to the other information set forth elsewhere in this Annual Report on Form 20-F, including our consolidated financial statements and the related notes beginning on page F-1, which could materially adversely affect our business, financial condition and future results. If any of the following risks actually occur, our business, financial condition and results of operations could be materially and adversely affected. In that event, the trading price of Purple Biotech's ordinary shares and American Depositary Shares could decline.

Risks Related to Our Financial Condition and Capital Requirements

We are a clinical-stage pharmaceutical company with a history of operating losses. We expect to incur significant additional losses in the future and may never be profitable.

We are a clinical-stage pharmaceutical company, and we are focused on the development and commercialization of innovative pharmaceutical drugs. We currently have two oncology therapeutic candidates in clinical trials, NT219 and CM24, neither of which has been approved for marketing and they are not being sold, marketed or commercialized, and a preclinical tribody platform with its leading therapeutic candidate, IM1240, which we acquired in connection with our acquisition of Immunorizon in February 2023. Each will require additional preclinical and/or clinical trials or other testing before we can obtain regulatory approval, if we are able to obtain regulatory approval at all. We must obtain regulatory approval for these therapeutic candidates, or any other therapeutic candidate that we may develop or acquire in the future before we can sell such therapeutic candidates. We have incurred losses from commencement of our pharmaceutical research and development activities through December 31, 2023, of approximately $137.5 million as a result of revenue and cost of goods, research and development activities, clinical trial related activities, investment/acquisition activities, listing for trading and fund-raising related activities, selling, general and administrative, finance expenses and other expenses. We may incur significant additional losses as we continue to focus our resources on advancing NT219, CM24, tribody platform with its leading therapeutic candidate IM1240 or other therapeutic candidates that we may develop, in-license, or acquire in the future. Our ability to generate revenue and achieve profitability depends mainly upon our ability, alone or with others, to successfully develop, in-license, or acquire, and obtain the required regulatory approvals for our oncology therapeutic candidates in the United States and various other territories and then to successfully commercialize our oncology therapeutic candidates. We may be unable to achieve any or all these goals with regard to NT219, CM24, tribody platform with its leading therapeutic candidate IM1240 or any other therapeutic candidates that we may develop, in-license, or acquire in the future. As a result, we may never be profitable or achieve significant or sustained revenues.

Our limited operating history as a pharmaceutical research and development company makes it difficult to evaluate our business and prospects, and we depend on the success of a limited portfolio of therapeutic candidates for our future revenue, which could impair our ability to achieve profitability.

We have a limited operating history as a pharmaceutical research and development company, and our operations to date have been limited primarily to developing our NT219 and CM24 therapeutic candidates and our tribody platform with its leading therapeutic candidate IM1240, as well as to developing, gaining regulatory approval and commercializing Consensi (prior to discontinuing related operations during 2021); research and development; raising capital; and recruiting scientific, CMC, regulatory and management personnel and third-party partners. To date, the only revenue we have received has been the initial milestone payments in connection with commercialization agreements for Consensi, which were terminated in 2021. We may not be able to commercialize or obtain regulatory approval for our NT219, CM24 and our tribody platform with its leading therapeutic candidate IM1240 therapeutic candidates or any additional therapeutic candidates we may develop, in-license and/or acquire in the future. Our future growth and success depend upon our ability to continue funding the development of our therapeutic candidates and on the successful commercialization of such therapeutic candidates. If we are unable to obtain regulatory clearances or approvals for our therapeutic candidates and future products, our ability to gain any revenues and to achieve profitability would be adversely affected. Consequently, any predictions about our future performance may not be accurate, and you may not be able to fully assess our ability to complete development of or commercialize our therapeutic candidates, acquire or in-license other therapeutic candidates, obtain regulatory approvals, or achieve market acceptance or favorable pricing for our therapeutic candidates.

We will need to raise additional capital to achieve our strategic objectives of developing and commercializing our therapeutic candidates, and to develop, acquire and/or in-license additional therapeutic candidates, and our failure to raise sufficient capital would significantly impair our ability to fund our future operations, develop our current or future therapeutic candidates, seek regulatory approval that is a prerequisite to selling any product, attract development or commercial partners and retain key personnel.

We will need to continue to expend substantial funds in research and development, including CMC, preclinical and clinical trials of our NT219, CM24 and our tribody platform with its leading therapeutic candidate IM1240 therapeutic candidates, as well as to acquire or in-license additional therapeutic candidates. We plan to fund our future operations through the out-licensing and/or commercialization of our therapeutic candidates and by raising additional capital through either debt or equity financing. However, we cannot be certain that we will be able to raise capital on commercially reasonable terms or at all, or that our actual cash requirements will not be greater than anticipated. We may have difficulty raising needed capital or securing a development or commercialization partner in the future as a result of, among other factors, our lack of revenues from commercialization of the therapeutic candidates, as well as the inherent business risks associated with our company and present and future market conditions. In addition, global and local economic and geopolitical conditions may make it more difficult for us to raise needed capital or secure a development or commercialization partner in the future and may impact our liquidity. If we are unable to obtain future financing, we may be forced to delay, reduce the scope of, or eliminate one or more of our research, development or commercialization programs related to our therapeutic candidates or any other therapeutic candidates that we may acquire, in-license or develop in the future, or to delay the acquisition or in-license of any additional therapeutic candidates, any of which may have a material adverse effect on our business, financial condition and results of operations.

On June 9, 2021, we entered into an open market sale agreement (the “Sales Agreement”), with Jefferies LLC (“Jefferies”), for the sale of ADSs, representing our ordinary shares. In accordance with the terms of the Sales Agreement, we may offer and sell, from time to time, ADSs through an “at-the-market” equity offering program (“ATM program”), with Jefferies acting as our agent. We originally filed a prospectus for a $50.0 million ATM program, but the aggregate offering price was subsequently reduced to $21.0 million on March 23, 2022, and to $3.0 million on October 17, 2023. Any future sales of ADS under the Sales Agreement could result in substantial dilution to existing shareholders. As of March 5, 2024, we have sold approximately 2,217,325 ADSs for total gross proceeds of $4.0 million under the Sales Agreement.

On December 8, 2022, we filed a registration statement on Form F-3 with the SEC utilizing a "shelf" registration process, under which we may offer and sell, from time to time in one or more offerings, up to an aggregate $200,000,000 of ADSs (representing our ordinary shares), ordinary shares, preferred shares, warrants, overallotment purchase rights, subscription rights, units and/or capital notes. In October 2023, we completed a $5 million registered direct offering with an institutional investor for the purchase and sale of 2,430,000 ADSs and pre-funded warrants to purchase up to 1,917,827 ADS, and, in a concurrent private placement, unregistered warrants to purchase up to 4,347,827 ADSs, which are exercisable immediately.

To the extent that we raise additional capital through the sale of equity, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic alliance and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates, or grant licenses on terms that are not favorable to us.

Our long-term capital requirements are uncertain and subject to numerous risks.

We estimate that so long as no significant revenues are generated from our oncology therapeutic candidates, we will need to raise substantial additional funds to develop and/or commercialize our therapeutic candidates and to develop, acquire or in-license any additional therapeutic candidates, as our current cash and short-term investments are not sufficient to complete the research and development of our therapeutic candidates in their current phase of development and any additional therapeutic candidates that we may acquire, in-license or develop in the future, and to fund our related expenses. Our long-term capital requirements are expected to depend on many potential factors, including, among others:

- the costs of seeking out and acquiring or engaging in-licensing or similar transactions for other oncological candidates;
- our ability to successfully complete the required CMC development for our oncology therapeutic candidates or any other therapeutic candidates that we may acquire, in-license, or develop in the future;
- our ability to successfully out-license and/or commercialize our oncology therapeutic candidates, or any other therapeutic candidates that we may acquire, in-license, or develop in the future, including securing commercialization agreements with third parties and favorable pricing and market share;
- the progress, success, and cost of our preclinical and/or clinical trials and research and development programs;
- the costs, timing and outcome of regulatory review and obtaining and maintaining regulatory approval of our oncology therapeutic candidates or any other therapeutic candidates that we may acquire, in-license, or develop in the future and addressing regulatory and other issues that may arise post-approval for such oncology therapeutic candidates;
- the costs of obtaining and enforcing our issued patents and defending intellectual property-related claims;
- the costs of developing and maintaining our third parties' cGMP manufacturing standards;
- our consumption of available resources more rapidly than currently anticipated, resulting in the need for additional funding sooner than anticipated;
- our ability to obtain recommendations and publish studies regarding the efficacy and/or safety of our oncology therapeutic candidates or any other therapeutic candidates that we may acquire or develop in the future that may be published by government agencies, professional organizations, academic or medical journals or other key opinion leaders; and
- sufficient coverage and reimbursement by third-party payers for our therapeutic candidates.

If we are unable to obtain approval, commercialize or out-license our oncology therapeutic candidates, or any other therapeutic candidates that we may acquire, in-license or develop in the future, maintain approval, or obtain future financing, we may be forced to delay, reduce the scope of, or eliminate one or more of our research and development programs related to the therapeutic candidates, which may have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Our Business, Operations and Regulatory Matters

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

The clinical trials of our therapeutic candidates are, and the manufacturing and marketing of our products will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and market our therapeutic candidates. Before obtaining regulatory approvals for the commercial sale of any of our therapeutic candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our therapeutic candidates are both safe and effective for use in each target indication. In particular, because some of our therapeutic candidates are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. The risk/benefit profile required for drug product approval will vary depending on these factors and may include not only the ability to show tumor shrinkage, but also adequate duration of response, a delay in the progression of the disease, and/or an improvement in survival. For example, response rates from the use of our therapeutic candidates may not be sufficient to obtain regulatory approval unless we can also show an adequate duration of response. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our therapeutic candidates may not be predictive of the results of later-stage clinical trials. The results of studies in one set of patients or line of treatment may not be predictive of those obtained in another. We expect that there may be greater variability in results for products processed and administered on a patient-by-patient basis, as anticipated for our therapeutic candidates, than for “off-the-shelf” products, like many other drugs. There is typically an extremely high rate of attrition from the failure of therapeutic candidates proceeding through clinical trials. Therapeutic candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. Many companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most therapeutic candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our therapeutic candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our therapeutic candidates.

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

Undesirable side effects or adverse events caused by our therapeutic candidates, or related to the combination therapies, 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 regulatory authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

If unacceptable toxicities arise in the development of our therapeutic candidates, the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our therapeutic candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment, or the ability of enrolled subjects to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. Any of these occurrences may harm our business, financial condition and prospects significantly.

If we and/or our potential commercialization partners are unable to obtain FDA and/or other foreign regulatory authority approval for our therapeutic candidates, we and/or our potential commercialization partners will be unable to commercialize our therapeutic candidates.

To date, we have not marketed, distributed or sold any oncology drug product. Our oncology therapeutic candidates are each subject to extensive governmental laws, regulations and guidelines relating to development, preclinical and clinical trials, manufacturing, and commercialization of drugs. We may not be able to obtain regulatory approval for any of our therapeutic candidates in a timely manner or at all.

Any material delay in obtaining, or the failure to obtain, required regulatory approvals will increase our costs and materially and adversely affect our ability to generate future revenues. Any regulatory approval to market a therapeutic candidate may be subject to restrictive conditions of use, including cautionary information, thereby limiting the size of the market for the therapeutic candidate. We also are, and will be, subject to numerous regulatory requirements from both the FDA and foreign state agencies that govern the conduct of preclinical and clinical trials, manufacturing and marketing authorization, pricing, and third-party reimbursement. Moreover, approval by one regulatory authority does not ensure approval by other regulatory authorities in separate jurisdictions. Each jurisdiction may have different approval processes and may impose additional testing requirements for our therapeutic candidates than other jurisdictions. Additionally, the FDA or other foreign regulatory bodies may change their approval policies or adopt new laws, regulations or guidelines in a manner that delays or impairs our ability to obtain the necessary regulatory approvals to commercialize our therapeutic candidates.

Preclinical studies, CMC, and clinical trials may involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future results. We and/or our potential commercialization partners will not be able to commercialize our therapeutic candidates without developing CMC satisfactory to regulatory authorities, completing preclinical and clinical studies, and then seeking to obtain regulatory approval, if such trials show that our therapeutic candidates are safe and effective.

We have limited experience in conducting and managing CMC, preclinical studies and clinical trials that are required to commence commercial sales of our therapeutic candidates. Developing and implementing CMC, and planning and conducting preclinical studies and clinical trials are expensive, complex, can take many years to complete and have uncertain outcomes. We cannot predict whether we, independently or through third parties, will encounter problems with any of the completed, ongoing or planned CMC, preclinical studies and/or clinical trials that will cause delays, including suspension of preclinical studies and/or clinical trials, delays in recruiting patients into the clinical trials, or delay of data analysis or release of the final report in our preclinical studies or clinical studies. Implementation of CMC and the preclinical studies and clinical trials of our therapeutic candidates may take significantly longer to complete than is estimated. Failure can occur at any stage of the testing, and we may experience numerous unforeseen events during, or as a result of, CMC, the preclinical studies and/or clinical trial process that could delay or prevent commercialization of our current or future therapeutic candidates.

In connection with CMC and the preclinical studies and clinical trials for our therapeutic candidates and other therapeutic candidates that we may seek to develop in the future, either on our own or through licensing or partnering agreements, we face various risks, including but not limited to:

- delays in manufacturing the drug substance and drug product for preclinical studies and clinical trials;
- delays in manufacturing the drug substance and drug product following NDA or BLA approval, if we receive such approval at all;
- delays in securing clinical investigators or trial sites for clinical trials that must be completed for us to obtain any approval that we seek;
- delays in receiving import or other government approvals to ensure appropriate drug supply, and shortages of combination drugs used in our clinical studies.
- delays in obtaining institutional review board (human ethics committee) and other regulatory approvals to commence a clinical trial;
- negative or inconclusive results from preclinical and/or clinical trials;
- the FDA or other foreign regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical studies and may not approve initiation of certain clinical trials;
- the clinical trials may be delayed or not completed due to the failure to recruit suitable candidates or if there is a lower rate of suitable candidates than anticipated or if there is a delay in recruiting suitable candidates;
- an inability to monitor patients adequately during or after treatment;

- problems with investigator or patient compliance with the trial protocols;
- a therapeutic candidate may not prove safe or efficacious;
- there may be unexpected or even serious adverse events and side effects from the use of a therapeutic candidate;
- the results with respect to any therapeutic candidate may not confirm the positive results from earlier preclinical studies or clinical trials;
- the results may not meet the level of statistical significance required by the FDA or other foreign regulatory authorities;
- the results will leave only limited and/or restrictive uses, including the inclusion of warnings and contraindications, which could significantly limit the marketability and profitability of the therapeutic candidate;
- our therapeutic candidates may not be reimbursed under different healthcare programs such as Medicare, Medicaid or private health insurance programs;
- changes to the current regulatory requirements related to clinical trials which can delay, hinder or lead to unexpected costs in connection with our receiving the applicable regulatory approvals; and
- the availability of other drugs that provide alternative and/or superior treatments to our drugs and therapeutic candidates.

A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after seeing promising results in earlier preclinical studies and/or clinical trials. As such, we do not know whether any clinical trials we may conduct will demonstrate adequate efficacy and safety sufficient to obtain regulatory approval to market our therapeutic candidates. If any of the preclinical studies and/or clinical trials of any therapeutic candidate do not produce favorable results, our ability to obtain regulatory approval for the therapeutic candidate may be adversely impacted, which will have a material adverse effect on our business, financial condition and results of operations.

If we do not establish collaborations for our oncology therapeutic candidates or any other therapeutic candidates that we may develop or acquire in the future, and/or commercialize such therapeutic candidates, or otherwise raise substantial additional capital, we will likely need to alter our development and any commercialization plans.

Our drug development programs, mainly the potential commercialization of our oncology therapeutic candidates, or any other therapeutic candidates that we may develop or acquire in the future, will require additional cash to fund expenses. As such, our strategy includes selectively partnering or collaborating with multiple pharmaceutical and biotechnology companies (including by way of out-licensing) to assist us in furthering development and potential commercialization of our therapeutic candidates, in some or all jurisdictions. We may not be successful in such collaborations with such third parties on acceptable terms, or at all. In addition, if we fail to negotiate and maintain suitable development (such as out-licensing) or commercialization agreements, we may have to limit the size or scope of our activities or we may have to delay one or more of our development or commercialization programs. Any failure to enter into or maintain development or commercialization agreements with respect to the development, marketing and commercialization of our therapeutic candidates in foreign jurisdictions where we do not have approval for commercialization, or any other therapeutic candidates that we may develop or acquire in the future, or failure to develop or acquire, market and commercialize such therapeutic candidates, will have an adverse effect on our business, financial condition and results of operation.

Any collaborative arrangements that we establish may not be successful or we may otherwise not realize the anticipated benefits from these collaborations. We do not control third parties with whom we have or may have collaborative arrangements, and we rely on them to achieve results which may be significant to us. In addition, any future collaboration arrangements may place the development, manufacturing and commercialization of our oncology therapeutic candidates or any other therapeutic candidates that we may develop or acquire in the future, outside our control, and may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

Our collaborative arrangements require us to rely on external consultants, advisors, experts and service providers for assistance in several key functions, including preclinical and clinical development, manufacturing, regulatory, market research, and intellectual property. We do not control these third parties, but we rely on them to achieve results, which may be significant to us. Our collaborative arrangements may not be successful or we may otherwise not realize the anticipated benefits from these collaborations. Additionally, we are responsible for any quality or regulatory issue that a collaborator may have that affects one or more of our therapeutic candidates. Relying upon collaborative arrangements to develop and/or commercialize our oncology therapeutic candidates or any other therapeutic candidates that we may develop or acquire in the future subjects us to a number of risks, including:

- we may not be able to control the amount and timing of resources that our collaborators may devote to our drug product or therapeutic candidates;
- we may be held liable should a collaborator fail to comply with applicable laws, rules, or regulations when performing services for us;
- our collaborators may experience financial difficulties or changes in business focus;
- our collaborators may experience quality or regulatory issues that negatively affect our therapeutic candidates;
- our collaborators may fail to secure adequate commercial supplies in a timely manner for our drug products upon marketing approval, if at all;
- we may suffer losses due to our collaborators' failure to perform their duties and we may not be able to be reimbursed by our collaborators for such losses;
- our collaborators may have a shortage of qualified personnel;
- we may be required to relinquish important rights, such as local trademark, marketing and distribution rights;
- business combinations or significant changes in a collaborator's business strategy may adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement;
- under certain circumstances, a collaborator could move forward with a competing therapeutic candidate developed either independently or in collaboration with others, including our competitors; and
- collaborative arrangements are often terminated or allowed to expire, which could delay and increase the cost of development of our therapeutic candidates.

If any of these or other scenarios materialize, they could have an adverse effect on our business, financial condition or results of operations.

Our current business model is based largely upon the development or acquisition and commercialization of new combination products and new therapeutic candidates that may have not yet been administered to humans or have limited history of treatment with humans. Unexpected difficulties or delays in successfully developing, acquiring or commercializing such combination and new drugs could have an adverse effect on our business, financial condition and results of operations.

We currently have two oncology therapeutic candidates in clinical trials, NT219 and CM24, both of which have limited safety and efficacy data for treatment in humans. The previous owners of CM24 conducted the first human clinical trials for this therapeutic candidate, which were initiated in 2015, and discontinued in 2017. In March 2021, we initiated a Phase 1b/2 clinical trial evaluating CM24, in advanced cancer patients, with expansion cohorts in subjects with non-small cell lung cancer (NSCLC) and pancreatic cancer, and in August 2022, we advanced the trial to a randomized, controlled, open label, multicenter Phase 2 study in subjects with metastatic pancreatic cancer (PDAC) as a second line treatment to evaluate the safety and tolerability of CM24 in combination with nivolumab and chemotherapy as compared to standard of care chemotherapy. In the second half of 2020, we commenced a first in human phase 1/2 study of NT219, as a single agent in patients with recurrent and/or metastatic advanced solid tumors, followed by a dose escalation phase of NT219 in combination with cetuximab for the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN) and colorectal adenocarcinoma. In February 2024, we determined the recommended Phase 2 dose (RP2D) for NT219 in combination with cetuximab in the treatment of head and neck cancer based on the Phase 1/2 dose escalation study to be 100mg/kg. We plan to commence a phase 2 study of NT219 at its RP2D level in combination with cetuximab in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck in the first half of 2024. Further, our third therapeutic candidate, IM1240, which is the leading therapeutic candidate of our tribody platform that we acquired in connection with our acquisition of Immunorizon in February 2023, is in preclinical development and no human clinical trials have been conducted for this therapeutic candidate. We cannot be certain whether any of our therapeutic candidates will be safe and efficacious when used in either monotherapy settings or in combination with other known cancer treatments.

In addition, we cannot be certain that the FDA or any foreign regulatory body will consider our oncology therapeutic candidates, whether alone or combined with other cancer treatments, or any other therapeutic candidate that we may develop or acquire in the future to be superior to the then current gold standard of care. Any delays in perfecting the combination, the production of the combination, or in market acceptance of the combination or new therapeutic candidates could have an adverse effect on our business, financial condition and results of operations.

Further, as part of our strategy for growth, we may consider the acquisition of additional therapeutic candidates at various stages of development and in a variety of therapeutic areas, and we may consider the acquisition or marketing rights of approved drug products as well. However, we may not be able to identify suitable acquisition candidates, complete acquisitions or integrate acquisitions successfully into our business. In this regard, acquisitions involve numerous risks, including difficulties in the integration of the acquired therapeutic candidates and/or drug product and the diversion of management's attention from other business concerns. For example, our ability to successfully transition and integrate the acquired Immunorizon may be critical for our future growth and financial stability, and given the challenges involved with the development of a biological product and the financial challenges, we may not be able to realize the anticipated benefits of the acquisition, which may materially adversely affect our growth and future operating results as well as our financial condition. Although we will endeavor to evaluate the risks inherent in any particular transaction, there can be no assurance that we will properly ascertain all such risks. In addition, acquisitions could result in the incurrence of substantial additional indebtedness and other expenses or in potentially dilutive issuances of equity securities. There can be no assurance that difficulties encountered with acquisitions will not have a material adverse effect on our business, financial condition and results of operations.

We rely mainly on third parties to conduct our CMC, research and development, preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including, but not limited to, failing to conform quality standards for our therapeutic candidates, which may endanger our clinical trial participants, and/or fail to meet established deadlines for the completion of such studies and trials.

We do not have the ability independently to conduct CMC, research and development, preclinical studies or clinical trials for our product candidates, and to a large degree we rely on third parties, such as contract manufacturing organizations, CROs, medical institutions, contract laboratories, current and potential development or commercialization partners, clinical investigators and independent study monitors, to perform these functions. Our reliance on these third parties for development activities reduces our control over these activities.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. Although we have, in the ordinary course of business, entered into agreements with these third parties, we continue to be responsible for confirming that each of our preclinical studies and clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the FDA and other regulatory agencies require us and our applicable third-party collaborators to comply with regulations and standards, commonly referred to as current good laboratory practices (cGLP), current good manufacturing practices (cGMP), and current good clinical practices (cGCP), for manufacturing and conducting, recording and reporting the results of preclinical and clinical trials to assure that data and reported results are credible and accurate and that the clinical trial participants are adequately protected. We cannot guarantee that our third-party collaborators will remain compliant with the applicable regulations. Regulatory authorities in other jurisdictions may have similar responsibilities and requirements. Our reliance on third parties does not relieve us of these responsibilities and requirements.

To date, we believe our contract manufacturing organizations, CROs and other third-party entities that support our manufacturing, research and development, preclinical or clinical practices with which we are working have generally performed well. However, if these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not meet our deadlines or 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, finding replacements may result in a delay of clinical trials and/or commercialization of products and additional costs. Accordingly, we may be delayed in obtaining regulatory approvals for our oncology therapeutic candidate or any therapeutic candidate that we may develop or acquire in the future, and we may be delayed in our efforts to successfully commercialize such therapeutic candidates for targeted diseases or fail to maintain marketing authorization to our drug products.

In addition, we rely substantially on third-party data managers for CMC and the preclinical study and clinical trial data that we present to regulatory authorities in order to obtain marketing authorizations. Although we attempt to audit and control the quality of third-party data, we cannot guarantee the authenticity or accuracy of such data, nor can we be certain that such data has not been fraudulently generated. There is no assurance that these third parties will pass FDA or regulatory audits, which could delay or prevent regulatory approval or cause revocation of already approved marketing authorization.

If third parties do not manufacture our current therapeutic candidates or any other therapeutic candidate that we may develop or acquire in the future in sufficient quantities in the required timeframe, at the required quality standards and at an acceptable cost, preclinical, clinical development and commercialization of our therapeutic candidates could be delayed.

We do not currently own or operate manufacturing facilities, and we rely, and expect to continue to rely, on third parties to manufacture preclinical, clinical and commercial quantities of our oncology therapeutic candidates or any other therapeutic candidate that we may develop or acquire in the future. Our reliance on third parties includes our reliance on them to manufacture such therapeutic candidates at a required standard of quality, including quality assurance related to regulatory compliance. Our current and anticipated future reliance upon others for the manufacture of our oncology therapeutic candidates or any other therapeutic candidate that we may develop or acquire in the future may adversely affect our future profit margins, if any, and our ability to develop such therapeutic candidates and commercialize any such therapeutic candidates at a required standard of quality and on a timely and competitive basis.

We may not be able to maintain our existing or future third-party manufacturing arrangements on acceptable terms, if at all. If for some reason our existing or future manufacturers do not perform as agreed or expected, or our existing or future manufacturers otherwise terminate their arrangements with us, we may be required to replace them. Although we are not entirely dependent upon our existing manufacturing agreements since we could replace them with other third-party manufacturers, we may incur added costs and delays in identifying, engaging, qualifying and training any such replacements, and in receiving regulatory approval for such replacements.

We rely on third-party contract vendors to manufacture and supply us with API/Drug Product to be compliant with the International Conference of Harmonization Q7 guidance and other applicable laws and regulations, in the quality and quantities we require on a timely basis.

We currently do not manufacture any API/Drug Product ourselves. Instead, we rely on third-party vendors for the manufacture and supply of our APIs/Drug Products that are used to formulate our oncology therapeutic candidates. While there are many potential API/Drug Product manufacturers and suppliers in the market, if these manufacturers or suppliers are incapable or unwilling to meet our current or future needs on acceptable terms or at all, or the current or future demand of the public, if any, we could experience delays in developing or conducting clinical trials for our current therapeutic candidates, NT219, CM24 and IM1240, or any other therapeutic candidate that we may develop or acquire in the future, and incur additional costs.

While there may be several alternative manufacturers or suppliers of API/Drug Product in the market, we have not conducted extensive audits and investigations into the quality or availability of their APIs/Drug Products. In addition, we may acquire therapeutic candidates which already have long term commitments to a specific API/Drug Product supplier. As a result, we can provide no assurances that supply sources will not be interrupted from time to time. Changing API/Drug Product manufacturers or suppliers or finding and qualifying new API/Drug Product manufacturers or suppliers can be costly and take a significant amount of time. Many APIs/Drug Products require significant lead time to manufacture. There can also be challenges in maintaining similar quality or technical standards from one manufacturing batch to the next.

If we are not able to find stable, reliable manufacturers or suppliers of our APIs/Drug Products, we may not be able to produce enough supplies of our oncology therapeutic candidates to meet our needs for further development and/or to conduct clinical trials, which could affect our business, financial condition and results of operation.

We anticipate continued reliance on third-party manufacturers if we are successful in obtaining marketing approval from the FDA and/or other regulatory agencies for NT219, CM24, our tribody platform's leading therapeutic candidate IM1240 or any other therapeutic candidates we may develop or acquire in the future.

To date, our NT219, CM24 and IM1240 therapeutic candidates have been manufactured in relatively small quantities by third-party manufacturers. Once our oncology therapeutic candidates and/or any other therapeutic candidate that we may develop or acquire in the future is approved for marketing and commercial sale, if at all, we still expect that we would continue to rely, at least initially, on third-party manufacturers to produce commercial quantities of such approved therapeutic candidates. These manufacturers may not be able to successfully increase the manufacturing capacity for any such therapeutic candidates that may be approved in the future 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. If we are unable to successfully increase the manufacturing capacity for our oncology therapeutic candidates or any therapeutic candidate that we may develop or acquire in the future, or we are unable to establish alternative manufacturing capabilities and in a timely manner, the commercial launch of any such therapeutic candidates that are approved in the future may be delayed or there may be a shortage in supply.

We and our third-party manufacturers are, and will be, subject to regulations of the FDA and other foreign regulatory authorities.

We and our third-party contract manufacturers are, and will be, required to adhere to laws, regulations and guidelines of the FDA and other foreign regulatory authorities setting forth cGMPs. These laws, regulations and guidelines cover all aspects of the manufacturing, testing, quality control and recordkeeping relating to our oncology therapeutic candidates when we initiate their clinical trials. We and our third-party contract manufacturers may not be able to comply with applicable laws, regulations and guidelines. We and our third-party contract manufacturers are and will be subject to unannounced inspections by the FDA, state regulators and similar foreign regulatory authorities outside the U.S. Our failure, or the failure of our third-party contract manufacturers, to comply with applicable laws, regulations and guidelines could result in the imposition of sanctions on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our therapeutic candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of our therapeutic candidates, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect regulatory approval and supplies of our therapeutic candidates and materially and adversely affect our business, financial condition and results of operations.

Our oncology therapeutic candidates and/or any other therapeutic candidate that we may develop or acquire in the future, if approved, will be subject to ongoing regulatory review. If we fail to comply with continuing U.S. and applicable foreign laws, regulations and guidelines, our clinical trials may be placed on hold, we could lose the FDA and/or other regulatory agencies' approval(s) we will obtain (if any), and our business would be seriously harmed.

If our oncology therapeutic candidates and/or any other therapeutic candidate that we may develop or acquire in the future receives regulatory approval to commercialize, such therapeutic candidate will be subject to ongoing post-marketing surveillance programs and regulatory review. We and our commercialization partners, as applicable, are subject to ongoing reporting obligations, including pharmacovigilance, or drug safety, and our manufacturing operations, and those of contract manufacturers that we select, will be subject to continuing regulatory review, including inspections by the FDA and other foreign regulatory authorities, if a product is approved for commercialization in such foreign jurisdictions. The results of this ongoing review may result in the withdrawal of an approved product from the market, the interruption of manufacturing operations or the imposition of labeling or marketing limitations. In addition, since many more patients are treated with drugs following their marketing post-approval, unanticipated adverse reactions or serious adverse reactions that were not observed in preclinical and/or clinical trials may be observed during the commercial marketing of a drug product.

As we move forward with commercializing drug products, we may also periodically discuss with the FDA and other regulatory authorities certain clinical, regulatory and manufacturing matters and, our views may, at times, differ from those of the FDA and other regulatory authorities. If we are required to conduct additional clinical trials or other testing of an approved drug product, we may face substantial additional expenses, and/or we have our approval to commercialize a drug product revoked by the FDA or a foreign regulatory body, should we obtain approval to commercialize in such foreign jurisdiction.

In addition, the manufacturer and the facilities that we or our commercialization partners use or may use to manufacture drug products in the future will be subject to periodic and unannounced review and inspection by the FDA and other foreign regulatory authorities. Later discovery of previously unknown problems with a drug product or a therapeutic candidate, the manufacturer or manufacturing process, or failure to comply with our post-approval requirements, rules and regulatory requirements, may result in actions such as:

- restrictions on such drug product, therapeutic candidate, manufacturer or manufacturing process;
- issuance of Form 483 inspection observations, untitled letters, warning letters from the FDA or other foreign regulatory authorities;

- withdrawal of the product or therapeutic candidate from the market;
- suspension or withdrawal of regulatory approvals;
- refusal to approve pending applications or supplements to approved applications that we or our potential commercialization partners submit;
- voluntary or mandatory recall;
- refusal to permit the import or export of our therapeutic candidates;
- product seizure or detentions;
- injunctions or the imposition of civil or criminal penalties and fines; or
- adverse publicity or changes to the drug's labeling.

The FDA or foreign regulatory authorities' policies may change, or additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our oncology therapeutic candidates. If we, or our current or potential commercialization partners, suppliers, third-party contractors or clinical investigators are slow to adapt, or are unable to adapt, to changes in existing regulatory requirements or the adoption of new regulatory requirements or policies, we or our potential commercialization partners may lose marketing approval for our oncology therapeutic candidates or any other therapeutic candidate that we may develop or acquire in the future, that obtain regulatory approval, resulting in decreased or lost revenue from milestones, product sales or royalties and could also result in other civil or criminal sanctions, including fines and penalties.

Regulatory approval of our oncology therapeutic candidates (if any) will be limited by the FDA and similar foreign authorities to those specific indications and conditions for which clinical safety and efficacy have been demonstrated, and the promotion of such product candidates for off-label uses, or in a manner that otherwise violates applicable FDA regulations, could adversely affect our business.

Any regulatory approval of therapeutic candidates is limited to those specific diseases and indications for which such therapeutic candidates have been deemed safe and effective by the FDA or similar foreign authorities. Marketing or commercializing of therapeutic candidates to treating a new symptom or indication, that was not approved by the FDA or similar foreign authorities would be considered promotion of off-label, or unapproved use, and would require us to file a supplemental new drug application and obtain regulatory approval. We will rely on physicians to prescribe and administer our therapeutic candidates (if approved for marketing by the FDA or similar foreign authorities) or as the product labeling directs and for the indications described on the labeling. To the extent any physicians prescribe such product to patients for off-label uses, or the use of such products depart from the approved use, this may increase the risk of injury or other adverse events to the patients and the risk of filing product liability claims against us. Product liability claims are expensive to defend regardless of merit and could result in substantial damage awards against us or harm our reputation. Furthermore, any off-label use may not effectively treat the conditions associated with such use, which could harm our reputation in the marketplace among physicians and patients, adversely affecting our operations.

While physicians may choose to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those approved by regulatory authorities, our ability to promote our therapeutic candidates (if approved for marketing by the FDA or similar foreign authorities) is limited to those indications that are specifically approved by the FDA or other regulatory authorities. Although regulatory authorities generally do not regulate the behavior of physicians, they do restrict communications by companies on the subject of off-label use. If the promotional activities related to our therapeutic candidates fail to comply with these regulations or guidelines, we may be subject to warnings from, or enforcement action by, the FDA or other regulatory authorities. In addition, failure to follow FDA rules and guidelines relating to promotion and advertising can lead to other negative consequences that could adversely affect our operations, such as the suspension or withdrawal of our therapeutic candidates from the market, enforcement letters, and corrective actions. Other regulatory authorities may impose separately penalties including, but not limited to, fines, disgorgement of money, operating restrictions, or criminal prosecution.

The FDA requires that our and our future distribution partners' sales and marketing efforts, as well as promotions, comply with various laws and regulations. Prescription drug promotions must be consistent with and not contrary to labeling, present "fair balance" between risks and benefits, be truthful and not false or misleading, be adequately substantiated (when required), and include adequate directions for use. In addition to the requirements applicable to approved drug products, we may also be subject to enforcement action in connection with any promotion of an investigational new drug. A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, may not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug candidate.

If the FDA investigates the marketing and promotional materials or other communications for our current or future commercial products and finds that any of our commercial products are being marketed or promoted in violation of the applicable regulatory restrictions, we and our distribution partners could be subject to FDA enforcement action. Any enforcement action (or related lawsuit, which could follow such action) brought against us in connection with alleged violations of applicable drug promotion requirements, or prohibitions, could harm our business and our reputation, as well as the reputation of any approved drug products we may promote or commercialize.

We may encounter substantial delays in the clinical trials for our therapeutic candidates, or we may not be able to conduct their trials on the timelines we expect, or we may not be able to complete them at all.

Clinical testing is expensive, time-consuming, and subject to uncertainty. Currently, two of our therapeutic candidates are in clinical trials, NT219 and CM24, and we cannot guarantee that any of these therapeutic candidate's and/or future therapeutic candidate's clinical studies will be initiated or conducted as planned, or completed on schedule, if at all. We intend to continue our clinical testing of CM24 and NT219, but issues may yet arise that could delay or prevent future clinical trials. A failure of one or more clinical studies can occur at any stage of testing, and clinical studies for any of our therapeutic candidates may not be successful. Events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical study site;
- the departure of a principal investigator from a clinical site, which could cause delays in conducting the clinical trial at a particular clinical site;
- the shortage of staff in the clinical sites;
- imposition of a temporary or permanent clinical hold by regulatory agencies;
- delays in recruiting suitable patients to participate in clinical studies for NT219, CM24 or future therapeutic candidates;
- failure by us or our CROs, or third parties, to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's cGCPs, requirements, or applicable regulatory guidelines in other countries;
- patients dropping out of a study;

- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;

- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;

- the cost of clinical studies of CM24 and NT219 and/or future therapeutic candidates being greater than we anticipate;

- management's decision to allocate internal resources to other projects;

- clinical studies of CM24, NT219 and/or future therapeutic candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring, conduct of additional clinical studies or abandon product development programs; and

- delays in manufacturing, testing, release, validating, or import/export of sufficient stable quantities of CM24, NT219, and/or future therapeutic candidates or approved drugs for use in clinical studies or the inability to do any of the foregoing, including any quality issues associated with contract manufacturers.

We also may conduct clinical research in collaboration with other biotechnology and biologics entities in which we combine CM24, NT219 and/or other or future therapeutic candidates with the technologies of such collaborators. Such collaborations may be subject to additional delays because of the management of the trials or the necessity of obtaining additional approvals for therapeutics used in the combination trials, or a shortage in the availability of such collaborators' drug products. These combination therapies will require additional testing and clinical trials, will require additional FDA regulatory approval, and will increase our future expenses.

In addition, if we make manufacturing or formulation changes to CM24, NT219 and/or other or future therapeutic candidates, we may be required, or may elect, to conduct additional studies to bridge the modified therapeutic candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to commercialize these therapeutic candidates successfully and may harm our business and the results of our operations.

A number of factors, including scheduling conflicts with participating clinicians and clinical institutions, and difficulties in identifying and enrolling patients who meet trial eligibility criteria, may cause significant delays in clinical studies. We may not commence or complete clinical trials involving any of our therapeutic candidates as projected or may not conduct them successfully.

We expect to rely on medical institutions, academic institutions, or CROs to conduct, supervise, or monitor some or all aspects of clinical trials involving our therapeutic candidates. If we fail to commence or complete, or experience delays in, any of its planned clinical trials, we may experience delays in its clinical development and/or commercialization plans.

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, among other things, 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 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 experience;
- competing clinical trials for similar therapies or other new therapeutics;
- clinicians' and patients' perceptions of the potential advantages and side effects of the product candidate being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will not complete a clinical trial; and
- the effect of epidemics, endemics or pandemics, such as the COVID-19 endemic, on the ability of patients to visit the testing sites and the effect of the disease on potential patients who contracted the disease.

Our clinical trials will compete with other clinical trials for therapeutic candidates that are in the same therapeutic areas as our therapeutic candidates, and this competition may reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Accordingly, we cannot guarantee that the trials will progress as planned or as scheduled. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing clinical trial and planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our therapeutic candidates.

Even if we can enroll a sufficient number of patients in our clinical trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our therapeutic candidates.

We may depend on a partner to conduct clinical trials with CM24, NT219 and/or other therapeutic candidates, and we may enter into future collaboration agreements with collaboration partners to develop and conduct clinical trials with, obtain regulatory approvals for, and to market and sell our therapeutic candidates. If such collaboration fails to perform as expected, our clinical trials and/or development plans will be delayed, and we will be required to seek other partners, which we may not be able to engage in a timely manner, if at all, and which may delay our development plans and therefore the potential for us to generate future revenue from our therapeutic candidates would be significantly reduced and our business would be significantly harmed.

We have entered into a clinical collaboration and supply agreement with Bristol Myers Squibb Company (NYSE:BMY) for a phase 1/2 study of CM24 in combination with a programmed cell death protein 1 (PD-1) antibody nivolumab, and an expansion study to also evaluate CM24 and nivolumab, together with nab-paclitaxel, in patients with pancreatic cancer. We initiated the phase 1b/2 portion of the phase 1/2 study in March 2021 and in August 2022, we initiated a randomized, controlled, open label, multicenter Phase 2 portion of this study in subjects with metastatic pancreatic cancer (PDAC) as a second line treatment to evaluate the safety and tolerability of CM24 in combination with nivolumab and chemotherapy and in December 2023, we enrolled the last patient for this Phase 2 study. We rely and may in the future continue to rely on our collaboration partners to develop, supply, conduct clinical trials, and/or commercialize our therapeutic candidates and approved products we may market in the future, if any. We may also enter into collaboration agreements with other parties in the future relating to such therapeutic candidates. Ultimately, if such therapeutic candidates are advanced through clinical trials, certain of the collaboration partners may have certain rights in connection with the commercialization of the therapeutic candidate, such as rights of first offer to be responsible for commercialization of these therapeutic candidates. If these collaboration partners do not perform in the manner we expect or fail to fulfill their responsibilities in a timely manner or at all, if the agreements with them terminate or if the quality or accuracy of the clinical data they obtain is compromised, the clinical development, regulatory approval and commercialization efforts related to our therapeutic candidates could be delayed or terminated, and it could become necessary for us to assume the responsibility at our own expense for the clinical development of such therapeutic candidates and seek replacement collaboration and/or development partners. In that event, we would likely be required to limit the size and scope of efforts for the development and commercialization of such product candidate; we would likely be required to seek additional financing to fund further development or identify alternative strategic collaboration partners; our potential to obtain regulatory approval for, and to generate future revenue from, such therapeutic candidates would be significantly reduced or delayed; and it could have a material adverse effect on our business, financial position, results of operations and future growth prospects.

Collaborations involving our therapeutic candidates pose a number of risks, including the following:

- collaboration partners have significant discretion in determining the efforts and resources that they will apply to these partnerships;
- collaboration partners may have limited supply of products, such as a PD-1 antibody, which we require for the development of our therapeutic candidates;
- collaboration partners may not perform their obligations as expected;
- collaboration partners may not pursue development of our therapeutic candidates or may elect not to continue or renew development programs, based on clinical trial results, changes in the collaboration partners' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaboration partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaboration partners may have or could independently develop, or develop with third parties, products that compete directly or indirectly with our out-licensed therapeutic candidates;
- disagreements with collaboration partners, including disagreements over proprietary rights, contract interpretation or the conduct of product research, development or commercialization programs, may cause delays or lead to termination of such programs, or require us to assume unplanned expenditures, responsibilities or liabilities with respect to therapeutic candidates we have out licensed, or may result in costly and time-consuming litigation or arbitration;
- collaboration partners may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaboration agreements may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable therapeutic candidates.

In addition, collaboration agreements may provide the collaboration partners with rights to terminate such agreements and licenses granted under such agreements under various conditions, which, if exercised, would adversely affect our product development efforts, could make it difficult for us to attract new collaboration partners and may adversely affect our reputation. Any such termination of any current or future agreement with a collaboration partner could have a material adverse effect on our business, financial position and results of operations.

The manufacture of our therapeutic candidates is complex, and we may encounter difficulties in production, particularly with respect to process development or scaling-up of our manufacturing capabilities. If we, or any of our third-party manufacturers encounter such difficulties, our ability to supply drugs for clinical trials or our products (if approved) for patients on a timely basis could be materially delayed or adversely affected. In addition, this may cause an increase in costs that could result in our inability to maintain a commercially viable cost structure.

NT219 is a small molecule chemical compound and CM24 and our tribody platform with its leading therapeutic candidate IM1240 are biologic compounds, and the process of manufacturing each is complex, highly regulated and subject to multiple risks. Even minor deviations from normal manufacturing processes for each of NT219, CM24 and our tribody platform with its leading therapeutic candidate IM1240 and/or any future therapeutic candidate could result in reduced production yields, product defects, and other supply disruptions.

Developing commercially viable processes is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency, and timely availability of raw materials. As a result of these challenges, we may experience delays in our therapeutic candidates' preclinical development, clinical development and/or commercialization plans. We may ultimately be unable to reduce the cost of goods for each of our therapeutic candidates to levels that will allow for an attractive return on investment if and when those therapeutic candidates are commercialized.

Because each of CM24, NT219 and our tribody platform with its leading therapeutic candidate IM1240 represents a novel approach to the treatment of disease, there are many uncertainties regarding the development, the market acceptance, third-party reimbursement coverage and the commercial potential of these therapeutic candidates.

There is no assurance that the approaches offered by CM24, NT219 or our tribody platform with its leading candidate IM1240 will gain broad acceptance among physicians or patients, or that governmental agencies or third-party medical insurers will be willing to provide reimbursement coverage for proposed therapeutic candidates. Since each of CM24, NT219 and our tribody platform with a leading therapeutic candidate IM1240 represents a new approach to treating various conditions, it may be difficult, in any event, to accurately estimate the potential revenues from these therapeutic candidates. Accordingly, we may spend large amounts of money trying to obtain approval for therapeutic candidates that have an uncertain commercial market. The market for any products that we may successfully develop utilizing our therapeutics candidates will also depend on the cost of the product. We do not yet have sufficient information to reliably estimate what it will cost to commercially manufacture these therapeutic candidates, and the actual cost to manufacture these therapeutic products could materially and adversely affect the commercial viability of these products. Our goal is to reduce the cost of manufacturing our therapeutic candidates. However, unless we reduce those costs to an acceptable amount, we may never be able to develop a commercially viable product. If we do not successfully develop and commercialize our therapeutic candidates based upon this approach or find suitable and economical sources for materials used in the production of these therapeutic candidates, these therapeutic candidates will not become profitable.

Our therapeutic candidates may be provided to patients in combination with other agents provided by third parties. The cost of such combination therapy may increase the overall cost of our therapeutic candidates' based therapies and may result in issues regarding the allocation of reimbursements between our therapeutic candidates and the other agents, all of which may adversely affect the ability to obtain reimbursement coverage for the combination therapy from third-party medical insurers.

If we fail to comply with any obligations under our in-license agreements with Yissum and/or THM or any future license agreement, or disputes arise with respect to those agreements, it could have a negative impact on our intellectual property rights and we could lose our rights to NT219 and/or CM24 or any future therapeutic candidate, which could have a material adverse effect on our business, financial condition and results of operation.

We are a party to a license agreement with each of Yissum, the technology transfer company of the Hebrew University of Jerusalem, and THM, pursuant to which we license rights to our therapeutic candidates NT219 and CM24, respectively. These license agreements impose, and we may enter into additional licensing arrangements with third parties that may impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Our rights to use the licensed intellectual property are subject to the continuation of and our compliance with the terms of these agreements. Disputes may arise regarding our rights to intellectual property licensed to us from a third-party, including but not limited to:

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

- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our ability to further license the technology to third parties;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected therapeutic candidates. If we fail to comply with our obligations under current or future licensing agreements or if other events occur that are not within our control, these agreements may be terminated or the scope of our rights under them may be reduced, we could lose the rights to our therapeutic candidates NT219 and CM24 or any other therapeutic candidate we license, and we might be unable to develop, manufacture or market any product that is licensed under these agreements, could experience delays in developing or commercializing these therapeutic candidates or incur additional costs, any of which could have a material adverse effect on our business, financial condition and results of operations.

In addition, we may have disputes over intellectual property rights related to our therapeutic candidates developed under service agreements or material transfer agreements with third parties. Such third parties may claim rights to certain know-how or intellectual property that may require us to enter into license agreements with such parties and pay royalties for such rights or to engage in legal proceedings with these parties.

Our shareholders may not realize a benefit from our acquisitions of therapeutic candidates commensurate with the ownership dilution they experienced in connection with the transactions.

If we are unable to realize the strategic and financial benefits anticipated from an acquisition (through the acquisition of a company or a company's assets), or in-licensing of therapeutic candidates, our shareholders may have experienced substantial dilution of their ownership interest without receiving any commensurate benefit. Due to the substantial number of the ADSs (including ADSs issuable upon exercise of the warrants to purchase ADSs) which were issued to shareholders in the acquisitions and the private placements we completed and may complete in the future in order to acquire our therapeutic candidates, the ownership stake and relative voting power of each ordinary share held by our previous shareholders was and may in the future be significantly reduced. Significant management attention and resources will be required to integrate and operate any acquired company or new product. Delays in this process could adversely affect our business, financial results, financial condition and price of our ordinary shares and/or ADSs following any acquisition or in-licensing agreement. Even if we are able to integrate the acquired business operations successfully, there can be no assurance that its integration will result in the realization of the full benefits of synergies, innovation, and operational efficiencies that may be possible from such integration and that the benefits will be achieved within a reasonable period of time.

For example, in February 2023 we completed the acquisition of 100% of the shares of Immunorizon, which is developing potential multi-specific T and NK cell engager oncology therapies that selectively activate the immune response within the tumor microenvironment (TME), in exchange for an aggregate upfront payment of $3.5 million in cash and an aggregate $3.5 million in ADSs (or 2,215,190 ADSs representing ordinary shares) and additional long-term milestones set at an aggregate amount of $94 million, with royalties out of net sales. While we have completed the process for the integration of Immunorizon's technology platform and allocated resources to the ongoing research and development related to the platform, given the challenges involved with the development of a biological product and the financial challenges, we may not be able to realize the anticipated benefits of the acquisition, which may materially adversely affect our growth and future operating results as well as our financial condition.

We depend on our ability to identify and acquire or in-license therapeutic candidates to achieve commercial success.

We own the rights to our therapeutic candidates, each of which was acquired by us from a third-party: NT219 (acquired in connection with the acquisition of the majority shareholdings of TyrNovo in 2017), CM24 (acquired in connection with the acquisition of FameWave in 2020) and tribody platform (acquired in connection with the acquisition of Immunorizon in February 2023). We evaluate internally and with external consultants each potential therapeutic candidate. However, there can be no assurance as to our ability to accurately or consistently select therapeutic candidates that have the highest likelihood to achieve commercial success.

Our business could suffer if we are unable to attract and retain key employees.

The loss of the services of members of senior management or other key personnel could delay or otherwise adversely impact the successful completion of our planned CMC, research and development, preclinical studies and/or clinical trials or the commercialization of our therapeutic candidates or otherwise affect our ability to manage our company effectively and to carry out our business plan. We do not maintain key-man life insurance for any of our personnel. Although we have entered into employment or consultancy agreements with every member of our senior management team, members of our senior management team may resign at any time. High demand exists for senior management and other key personnel in the pharmaceutical industry. There can be no assurance that we will be able to continue to retain and attract such personnel.

Our growth and success also depend on our ability to attract and retain additional highly qualified scientific, technical, business development, marketing, managerial and finance personnel. If we purchase or in-license new products or product candidates, we may need to expand our qualified personnel to advance the development and commercialization of such products. In addition, if we elect to independently commercialize any therapeutic candidate, we will need to expand our marketing and sales capabilities. We experience intense competition for qualified personnel, and the existence of non-competition agreements between prospective employees and their former employers may prevent us from hiring those individuals or subject us to liability from their former employers. While we attempt to provide competitive compensation packages to attract and retain key personnel, many of our competitors are likely to have greater resources and more experience than we have, making it difficult for us to compete successfully for key personnel. Compensation packages for our senior officers are subject to approval of our compensation committee and board of directors (the “Board”) and, in certain instances, our shareholders. We may not be able to achieve the required corporate approvals for proposed compensation packages, further making it difficult for us to compete successfully with other companies to attract and retain key personnel. If we cannot attract and retain sufficiently qualified technical employees on acceptable terms, we may not be able to develop and commercialize competitive therapeutic candidates. Further, any failure to effectively integrate new personnel could prevent our business from successfully growing.

We are an international business, and we are exposed to various global and local risks that could have an adverse effect on our business.

We operate our business in multiple international jurisdictions. Such operations could be affected by changes in foreign exchange rates, capital and exchange controls, travel restrictions, public health restrictions, expropriation and other restrictive government actions, changes in intellectual property legal protections and remedies, trade regulations and procedures and actions affecting approval, production, export and import of pharmaceutical products, pricing, and marketing of, reimbursement for and access to, our products, as well as by political unrest, unstable governments and legal systems and inter-governmental disputes. Any of these changes could adversely affect our business.

Our subsidiary, TyrNovo, has received Israeli governmental grants to assist in the funding of its research and development activities. The IIA grants which TyrNovo's technology, including NT219, has received for research and development expenditures restrict its ability to manufacture products and transfer (including by way of license for R&D purposes) know-how outside of Israel and require it to satisfy specified conditions. In addition, we may encounter difficulties partnering TyrNovo's therapeutic candidates with entities outside of Israel due to certain restrictions regarding manufacturing and transferring of know-how (including by a way of license for R&D purposes) outside of Israel imposed due to the receipt of the IIA grants.

TyrNovo's technologies, including NT219, were developed, in part, with grants from the Israel Innovation Authority, or IIA (formerly known as the Office of the Chief Scientist of the Ministry of Economy and Industry) in the aggregate amount of approximately NIS 5.5 million (or approximately $1.5 million). As of December 31, 2023, TyrNovo had not paid any royalties to the IIA and had a contingent obligation to the IIA (including interest) of $2.3 million. The requirements and restrictions for such grants are set forth in the Encouragement of Research, Development and Technological Innovation in Industry Law, 5744-1984 (formerly known as the Law for the Encouragement of Research and Development in Industry, 5744-1984), or the Innovation Law, the IIA's rules and guidelines and the terms of these grants.

In general, the recipients of IIA grants are obligated to pay the IIA royalties from the revenues generated from the sale of products and related services developed as a result of a research and development program funded, in whole or in part, by the IIA, at rates which are determined under the IIA's rules and guidelines (generally of 3% to 6% on sales of products or services developed under the approved programs, which rates may be increased under certain circumstances) up to the aggregate amount of the total grants received by the IIA (which may be increased under certain circumstances, as described below), plus annual interest (as determined in the IIA's rules and guidelines). Following the full payment of such royalties and interest, there is generally no further liability for royalty payments; however, other restrictions under the Innovation Law continue to apply, as described below.

Under the IIA's rules and guidelines, TyrNovo is generally prohibited from manufacturing products developed using the IIA funding outside of the State of Israel without the prior approval of the IIA (except for the transfer of less than 10% of the manufacturing capacity in the aggregate which requires only a notice) and subject to payment of increased royalties (up to 300% of the grant amount plus accrued interest, depending on the manufacturing volume that is performed outside of Israel). TyrNovo received the IIA's approval for the production of NT219's API and final product by certain third-party manufacturers outside of Israel in consideration for (among other things) the future payment of increased royalties as stipulated under the IIA's rules and guidelines. Additionally, under the IIA's rules and guidelines, TyrNovo is prohibited from transferring the IIA-funded know-how and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the prior approval of the IIA. TyrNovo may not receive the required approvals for any proposed transfer, and even if received, TyrNovo may be required to pay the IIA a redemption fee of up to 600% of the grant amounts plus accrued interest. Approval of the transfer of know-how to an Israeli company is also required, and may be granted if the recipient assumes all of our responsibilities towards the IIA, including the restrictions on the transfer of know-how and the manufacturing rights outside of Israel and the obligation to pay royalties, and, although such transfer will not be subject to the payment of a redemption fee, there will be an obligation to pay royalties to the IIA from the income of such sale transaction as part of the royalty payment obligation. No assurance can be given that approval to any such transfer, if requested, will be granted.

These restrictions may impair our ability to perform or outsource manufacturing outside of Israel, or otherwise transfer or sell TyrNovo's IIA funded know-how outside of Israel. Furthermore, the consideration available to TyrNovo's and/or our shareholders in a transaction involving the transfer outside of Israel of know-how developed with IIA funding (such as a merger or similar transaction) may be reduced by any amounts that TyrNovo is required to pay to the IIA. If TyrNovo fails to comply with the requirements of the Innovation Law and the IIA's rules and guidelines, TyrNovo may be required to return certain grants previously received along with interest and penalties and may become subject to criminal proceedings.

We have in the past, and may in the future, become subject to litigation or claims arising in or outside the ordinary course of business that could negatively affect our business operations and financial condition.

We have in the past, and may in the future, become subject to litigation or claims arising in or outside the ordinary course of business (other than intellectual property infringement actions) that could negatively affect our business operations and financial condition, including securities class actions and shareholder derivative actions, both of which are typically expensive to defend. Such claims and litigation proceedings may be brought by third parties, including our competitors, advisors, service providers, partners or collaborators, employees, and governmental or regulatory bodies. For information on past legal proceedings, please see "Item 8. Financial Information – A. Financial Statements and Other Financial Information – Legal Proceedings." Any claims and lawsuits, and the disposition of such claims and lawsuits, could be time-consuming and expensive to resolve, divert management attention and resources, and lead to attempts on the part of other parties to pursue similar claims. We may not be able to determine the amount of any potential losses and other costs we may incur due to the inherent uncertainties of litigation and settlement negotiations. In the event we are required or decide to pay amounts in connection with any claims or lawsuits, such amounts could be significant and could have a material adverse impact on our liquidity, business, financial condition and results of operations. In addition, depending on the nature and timing of any such dispute, a resolution of a legal matter could materially affect our future operating results, our cash flows or both. Additionally, we may be unable to maintain our existing directors' and officers' liability insurance in the future at satisfactory rates or adequate coverage amounts and may incur significant increases in insurance costs.

Risks Related to Our Industry

Even if our oncology therapeutic candidates or any other therapeutic candidate that we develop or in-license in the future receive regulatory approval, they may not become or remain commercially viable products.

In the event that our oncology therapeutic candidates and/or any other therapeutic candidate that we may develop or acquire in the future are approved for commercialization by the FDA or a foreign authority, they may not be commercially viable products. For example, if we or our potential commercialization partners receive regulatory approval to market a therapeutic candidate, approval may be subject to limitations on the indicated uses or subject to labeling or marketing restrictions which could materially and adversely affect the marketability and profitability of the therapeutic candidate. In addition, a new therapeutic candidate may appear promising at an early stage of development or after preclinical studies and/or clinical trials but never reach the market, or it may reach the market but not result in sufficient product sales, if any. A therapeutic candidate may not result in commercial success for various reasons, including:

- difficulty in large-scale manufacturing, including yield and quality;
- low market acceptance by physicians, healthcare payers, patients and the medical community as a result of lower demonstrated clinical safety or efficacy compared to other products, prevalence and severity of adverse side effects, or other potential disadvantages relative to alternative treatment methods;
- insufficient or unfavorable levels of reimbursement from government or third-party payers, such as insurance companies, health maintenance organizations and other health plan administrators;
- infringement on proprietary rights of others for which we or our potential commercialization partners have not received licenses;

- incompatibility with other therapeutic candidates;
- other potential advantages of alternative treatment methods and competitive forces that may make it more difficult for us to penetrate a particular market segment;
- ineffective marketing and distribution support;
- lack of significant competitive advantages over existing products on the market;
- lack of cost-effectiveness; or
- timing of market introduction of competitive products.

If we are unable, either on our own or through third parties, to manufacture, commercialize and market our oncology therapeutic candidates or any other therapeutic candidates that we may develop or acquire in the future when planned, or develop or acquire commercially viable therapeutic candidates, we may not achieve any market acceptance or generate revenue.

The markets for our oncology therapeutic candidates are rapidly changing and competitive, and new drug delivery mechanisms, drug delivery technologies, new drugs and new treatments which may be developed by others could impair our ability to maintain and grow our business and remain competitive.

The pharmaceutical and biotechnology industry is highly competitive, and we face significant competition from many pharmaceutical, biopharmaceutical and biotechnology companies that are researching and marketing products designed to address the indications treated by our oncology therapeutic candidates. There are various other companies that currently market or are in the process of developing products that address all of the indications or diseases treated by our therapeutic candidates, some of them are in a more progressed stage of development than us and may reach the market before we do.

New drug delivery mechanisms, drug delivery technologies, new drugs and new treatments that have been developed or that are in the process of being developed by others may render our oncology therapeutic candidates noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Some of these technologies may have an entirely different platform or means of treating the same indications as NT219, CM24, our tribody platform with its leading therapeutic candidate IM1240 or other therapeutic candidates that we may develop or in-license in the future. Technological competition from pharmaceutical and biotechnology companies, universities, governmental entities and others, is intense and is expected to increase. Many of these entities have significantly greater research and development capabilities, human resources and budgets than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors' financial, marketing, manufacturing and other resources.

The potential widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our formulations or therapeutic candidates, even if commercialized. Many of our targeted diseases and conditions can also be treated by other medications or drug delivery technologies. These treatments may be widely accepted in medical communities and have a longer history of use. The established use of these competitive drugs may limit the potential for our oncology therapeutic candidates to receive widespread acceptance.

If third-party payers do not adequately reimburse customers for our oncology therapeutic candidates, if approved for marketing in the U.S. or other markets, they might not be purchased or used, and our revenues and profits will not develop or increase.

Our revenues and profits will depend heavily upon the availability of adequate coverage and reimbursement for the use of our oncology therapeutic candidates, if approved, from governmental and/or other third-party payers, both in the U.S. and in foreign markets. There may be significant delays in obtaining coverage for newly approved therapeutic candidates. Moreover, eligibility for coverage does not necessarily signify that an approved product will be reimbursed in all cases or at a sufficient rate, including one that covers our costs, such as research, development, manufacture, sale, and distribution costs. Accordingly, even if we succeed in bringing one or more of our therapeutic candidates to the market, they may not be considered cost-effective, and the amount reimbursed may be insufficient to allow us to sell our approved products on a competitive basis. Reimbursement by a third-party payer may depend upon a number of factors, including the third-party payer's determination that the use of an approved product is, among others:

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

Obtaining reimbursement approval for an approved product from each government or other third-party payer is a time-consuming and costly process that could require us or our current or potential development and commercialization partners to provide supporting scientific, clinical and cost-effectiveness data for the use of an approved product to each payer. Even when a payer determines that an approved product is eligible for reimbursement, the payer may impose coverage limitations that preclude or restrict payment for some uses that are approved by the FDA or other foreign regulatory authorities. Reimbursement rates may vary according to the use of the approved product and the clinical setting in which it is used, may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints or imperfections in Medicare, Medicaid or other data used to calculate these rates.

Increasingly, the third-party payers who reimburse patients or healthcare providers, such as government and private insurance plans, are seeking greater upfront discounts, additional rebates, and other concessions to reduce the prices for approved products. If the price we are able to charge for any approved product, or the reimbursement provided for such approved product, is inadequate or becomes inadequate in light of our development and other costs, our return on investment could be adversely affected.

In the U.S., there have been, and we expect that there will continue to be, federal and state proposals to constrain expenditures for medical products and services which may affect payments for our oncology therapeutic candidates, if approved. We believe that legislation that reduces reimbursement for our oncology therapeutic candidates, if approved, could adversely impact how much or under what circumstances healthcare providers will prescribe or administer our oncology therapeutic candidates, if approved. This could materially and adversely impact our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our oncology therapeutic candidates, if approved. At this stage, we are unable to estimate the extent of the direct or indirect impact of any such federal and state proposals.

Further, coverage and reimbursement policies are subject to change and are not always consistent across different payers or even federal healthcare programs. For example, the Centers for Medicare and Medicaid Services (CMS) frequently change product descriptors, coverage policies, product and service codes, payment methodologies and reimbursement values which may be revised or interpreted in ways that could significantly affect our business and products. Government and private third-party payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Moreover, both CMS and other third-party payers may have sufficient market power to demand significant price reductions. Such price reductions and/or other significant coverage policies or payment limitations could materially and adversely affect our business, financial condition and results of operations.

Legislative or regulatory reform of the healthcare system in the United States may harm our business.

On March 23, 2010, President Obama signed the "Patient Protection and Affordable Care Act" (P.L. 111-148) (the "ACA") and on March 30, 2010, he signed the "Health Care and Education Reconciliation Act" (P.L. 111-152), collectively commonly referred to as the "Healthcare Reform Law." The Healthcare Reform Law included a number of new rules regarding health insurance, the provision of healthcare, conditions to reimbursement for healthcare services provided to Medicare and Medicaid patients, and other healthcare policy reforms. Through the law-making process, substantial changes have been and continue to be made to the current system for paying for healthcare in the U.S., including changes made to extend medical benefits to certain Americans who lacked insurance coverage and to contain or reduce healthcare costs (such as by reducing or conditioning reimbursement amounts for healthcare services and drugs, and imposing additional taxes, fees, and rebate obligations on pharmaceutical and medical device companies). This legislation was one of the most comprehensive and significant reforms ever experienced by the U.S. in the healthcare industry and has significantly changed the way healthcare is financed by both governmental and private insurers. This legislation has impacted the scope of healthcare insurance and incentives for consumers and insurance companies, among others. Additionally, the Healthcare Reform Law's provisions were designed to encourage providers to find cost savings in their clinical operations. Pharmaceuticals represent a significant portion of the cost of providing care. This environment has caused changes in the purchasing habits of consumers and providers and resulted in specific attention to the pricing negotiation, product selection and utilization review surrounding pharmaceuticals which could result in lower pricing and/or reduced market acceptance for any drug products we may commercialize in the U.S. in the future. At this stage, it is difficult to estimate the full extent of the direct or indirect impact of the Healthcare Reform Law on us.

Further, the healthcare regulatory environment has seen significant changes in recent years and is still in flux. Legislative initiatives to modify, limit, replace, or repeal the ACA and judicial challenges have continued for over a decade. However, as of the Supreme Court's ruling ordering the dismissal of, arguably, the most promising case challenging the ACA to-date on June 17, 2021, it appears that the ACA 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 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 ACA 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 ACA. 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 August 2022, the Inflation Reduction Act ("IRA") was signed into law, which will, among other things, allow U.S. Department of Health and Human Services ("HHS") to negotiate the selling price of certain drugs and biologics that the Centers for Medicare & Medicaid Services ("CMS") reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price. Beginning in October 2023, the IRA also began penalizing drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. Additionally, in December 2023, the Biden-Harris Administration announced further related initiatives under the IRA to lower prescription costs and increase competition with help from HHS, the DOJ, and the FTC.

There is uncertainty as to what healthcare programs and regulations may be implemented or changed at the federal and/or state level in the U.S. or the effect of any future legislation or regulation. However, in early January 2024, the FDA did approve a plan from Florida to import low-cost drugs from Canada. Furthermore, we cannot predict what actions the Biden administration will implement in connection with the Health Reform Law. However, it is possible that such initiatives could have an adverse effect on our ability to obtain approval and/or successfully commercialize products in the U.S. in the future, as applicable.

We are subject to additional federal and state healthcare laws and regulations relating to our business, and our failure to comply with those laws could have a material adverse effect on our results of operations and financial conditions.

Healthcare providers, physicians, and third-party payers play a primary role in the recommendation and prescription of any therapeutic candidates for which we obtain marketing approval. Our current or future arrangements with healthcare providers, physicians, marketers or sales personnel, third-party payers, patients, and others in a position to refer, recommend, purchase, or use our products may expose us to broadly applicable U.S. federal and state fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we obtain FDA approval. The applicable healthcare laws to which we have been and/or may be subject include, but are not limited to, the following:

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

- the federal Anti-Inducement Law (also known as the Civil Monetary Penalties Law), which prohibits a person from offering or transferring remuneration to a Medicare or State healthcare program beneficiary that the person knows or should know is likely to influence the beneficiary’s selection of a particular provider, practitioner or supplier of any item or service for which payment may be made, in whole or in part, by Medicare or a State healthcare program;

- the Ethics in Patient Referrals Act of 1989, commonly referred to as the Stark Law, which prohibits physicians from referring Medicare or Medicaid patients for certain designated health services where that physician or family member has a financial relationship with the entity providing the designated health service, unless an exception applies;

- federal false claims laws that prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other government healthcare programs that are false or fraudulent;

- the so-called federal “Sunshine Act”, which requires certain pharmaceutical and medical device companies to monitor and report certain payments and other transfers of value to physicians, as defined by such law, certain other healthcare professionals, and teaching hospitals and ownership and investment interests held by physicians and their immediate family members to CMS for disclosure to the public;

- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its implementing regulations, which impose obligations on certain covered entities and their business associates with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals, regulatory authorities, and potentially the media of certain breaches of security of individually identifiable health information;

- HIPAA’s fraud and abuse provisions, which impose criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the federal Food, Drug, and Cosmetic Act, which, among other things, strictly regulate drug product and medical device marketing, prohibits manufacturers from marketing such products for off-label use, and regulates the distribution of samples;

- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; and

- state law equivalents of each of the above federal laws, such as anti-kickback, false claims, transparency and reporting laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, many of which differ from each other in significant ways, thus complicating compliance efforts.

Compliance efforts may involve substantial costs and resources, and if our operations or business arrangements are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful.

Most recently, there has been a trend in federal and state legislation aimed at lowering costs for drug products, including by requiring pharmaceutical companies to disclose information about their pricing and production and marketing costs, and heightened governmental scrutiny over the manner in which pharmaceutical manufacturers set prices for their marketed products. There have been several presidential executive orders and U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, on October 10, 2018, the Patient Right to Know Drug Prices Act (for private plans) and the Know the Lowest Price Act (for Medicare Parts C and D) were signed into law, which prohibited health plans from restricting pharmacies from informing individuals regarding prices for certain drugs. On November 20, 2020, the U.S. Department of Health and Human Services finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed in response to ongoing litigation. In addition, in November 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. Given resulting litigation and preliminary injunctions that were issued, the rule was not implemented and will not be implemented without further rulemaking. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. For example, in June 2016 Vermont became the first state to pass legislation requiring certain drug companies to disclose information relating to justification of certain price increases, and many other states have since followed suit. These efforts and any other such legislation requiring publication of drug costs could materially and adversely impact our business, financial condition, and results of operations by promoting a reduction in drug prices or encouraging purchasers to use other low-cost, established drugs or therapies.

In addition, there has been a trend of increased federal and state regulation of payments made to physicians or others in a position to refer, purchase, or recommend drug products. For example, some states impose a legal obligation on companies to adhere to voluntary industry codes of behavior (e.g., the PhRMA Code), which apply to pharmaceutical companies' interactions with healthcare providers, some mandate implementation of corporate compliance programs, along with the tracking and reporting of gifts, compensation, and other remuneration to physicians, and some states limit or prohibit such gifts. Further, the Healthcare Reform Law, among other things, amended the intent requirement of the federal Anti-Kickback Statute so that a person or entity can now be found guilty of fraud or an anti-kickback violation without actual knowledge of the statute or specific intent to violate it. In addition, the Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statue constitutes a false or fraudulent claim for purposes of the False Claims Act.

The scope and enforcement of these laws are broad, often uncertain and subject to change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and guidance in many areas. We cannot predict the impact that new legislation or any changes in existing legislation will have on our business, financial condition, or results of operations. Federal or state regulatory authorities may challenge our prior and/or future activities under these laws. Any such challenge could have a material adverse effect on our reputation, business, results of operations, and financial condition. Any state or federal regulatory review of us, regardless of the outcome, would be costly and time-consuming and could negatively and adversely affect our business and results of operations.

We could be exposed to significant drug product liability claims, which could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage.

The clinical trials that we conduct, conducted or may have to conduct, and the testing, manufacturing, marketing and commercial sale of our oncology therapeutic candidates or any other therapeutic candidates that we may develop or acquire in the future, involve and will involve an inherent risk that significant liability claims may be asserted against us. Should we decide to seek additional insurance against such risks before we initiate clinical trials or commence our product sales, there is a risk that such insurance will be unavailable to us, or if it can be obtained at such time, that it will be available only at an unaffordable cost. Even if we obtain insurance, it may prove inadequate to cover claims or litigation costs, especially in the case of wrongful death claims. Product liability claims or other claims related to our therapeutic candidates or any other therapeutic candidate that we may develop or acquire in the future, regardless of their outcome and merit, could require us to spend significant time and money in litigation or to pay significant settlement amounts or judgments. Any successful product liability or other claim may prevent us from obtaining adequate liability insurance in the future on commercially desirable or reasonable terms. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our therapeutic candidates or any other therapeutic candidates that we may develop or acquire in the future. A product liability claim could also significantly harm our reputation and delay market acceptance of our therapeutic candidates or any other therapeutic candidate that we may develop or acquire in the future.

Our business involves risks related to handling regulated substances which could severely affect our ability to conduct research and development of our therapeutic candidates.

In connection with our current or potential development and commercialization partners' research and clinical development activities, as well as the manufacture of materials and therapeutic candidates, we and our current or potential development and commercialization partners are subject to foreign, federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. We and our current or potential development and commercialization partners may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and clinical development, as well as the activities of our manufacturing and current or potential development and commercialization partners, both now and in the future, may involve the controlled use of hazardous materials, including but not limited to certain hazardous chemicals. We cannot eliminate the risk of accidental contamination or injury from these materials. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

Unfavorable macroeconomic conditions and other adverse macroeconomic factors could adversely affect our business, financial condition, cash flow or results of operations.

Unfavorable macroeconomic conditions and other adverse macroeconomic factors have resulted, among other matters, in tightening in the debt and equity markets, and high levels of inflation. For example, tightening of the equity markets, makes it more difficult to raise capital at a reasonable valuation or at all. In addition, the U.S. Bureau of Labor Statistics has reported for the period from January 2022 to January 2023, the Consumer Price Index for All Urban Consumers rose 6.4 percent, and from January 2023 to January 2024, the Consumer Price Index for All Urban Consumers rose 3.1 percent. If the inflationary pressure continues for a prolonged period, it may continue to result in increased costs of labor, cost of clinical trials, and costs of manufacturing which could adversely affect our results of operations. Furthermore, during 2022 and 2023 there was a significant increase in interest rates that impacted the cost of debt, liquidity and valuations of companies and other assets. Our results of operations could be adversely affected by general conditions in the global and local macroeconomic economy conditions affecting the financial markets. An economic downturn could result in a variety of risks to our business, including weakened demand for our therapeutic candidates and our inability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our partners and suppliers, possibly resulting in supply disruption, or cause future customers to delay making payments for our products. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our business and operations may be materially adversely affected in the event of computer system failures or security or breaches due to cyber-attacks or cyber intrusions, including ransomware, phishing attacks and other malicious intrusions.

In recent years, cybersecurity threats have become a greater risk and focus for companies. In particular, ransomware attacks, where a hacker locks and threatens to delete or disclose the victim's data unless a ransom is paid, has become a major risk. We and those of our third-party contract manufacturers and other third parties on which we rely are at risk of cyber-attacks or cyber intrusions via the Internet, computer viruses, break-ins, malware, ransomware, phishing attacks, hacking, denial-of-service attacks or other attacks and similar disruptions from the unauthorized use of, or access to, computer systems (including from internal and external sources). These types of incidents continue to be prevalent and pervasive across industries, including in our industry. In addition, we expect information security risks to continue to increase due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors.

Despite the implementation of security measures, our internal computer systems, and those of our third-party contract manufacturers and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber-attacks, cyber intrusions, natural disasters, fire, terrorism, war, and telecommunication and electrical failures. If such an event were to occur and interrupt our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, we could incur liability and the further development of our therapeutic candidates could be delayed.

Increasing scrutiny of, and evolving expectations for, sustainability and environmental, social, and governance ("ESG") initiatives could increase our costs or otherwise adversely impact our business.

Public companies are facing increasing scrutiny related to ESG practices and disclosures from certain investors, capital providers, shareholder advocacy groups, other market participants and other stakeholder groups. For example, certain institutional and individual investors have requested various ESG-related information and disclosures as they increasingly incorporate ESG criteria in making investment and voting decisions. With this increased focus, public reporting regarding ESG practices is becoming more broadly expected. Such increased scrutiny may result in increased costs, enhanced compliance or disclosure obligations, or other adverse impacts on our business, financial condition or results of operations. If our ESG practices and reporting do not meet investor or other stakeholder expectations, which continue to evolve, we may be subject to investor or regulator engagement regarding such matters. In addition, new sustainability rules and regulations have been adopted and may continue to be introduced in various states and other jurisdictions. For example, the SEC has published proposed rules that would require companies to provide significantly expanded climate-related disclosures in their periodic reporting, which may require us to incur significant additional costs to comply and impose increased oversight obligations on our management and Board. Our failure to comply with any applicable rules or regulations could lead to penalties and adversely impact our reputation, access to capital and employee retention. Such ESG matters may also impact our third-party contract manufacturers and other third parties on which we rely, which may augment or cause additional impacts on our business, financial condition, or results of operations.

Risks Related to Intellectual Property

Third-party claims of intellectual property infringement and other legal challenges may require us to spend substantial time and money and could prevent us from or delay us in developing or commercializing our therapeutic candidates. An adverse result in any infringement claims or other legal challenges could have a material adverse effect on our business, results of operations and on our financial condition.

The development, manufacture, use, offer for sale, sale or importation of our therapeutic candidates may infringe on the claims of third-party patents or other intellectual property rights. The nature of claims contained in unpublished patent filings around the world is unknown to us, and it is impossible to know which countries patent holders may choose for the extension of their filings under the Patent Cooperation Treaty, or other mechanisms. We may also be subject to claims based on the actions of employees and consultants with respect to the usage or disclosure of intellectual property learned at other employers. The cost to us of any intellectual property litigation or other infringement proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation or defense of intellectual property litigation or other legal proceedings or litigation could have a material adverse effect on our ability to compete in the marketplace. Intellectual property litigation and other proceedings may also absorb significant cash resources and management attention and time. Consequently, we are unable to guarantee that we will be able to manufacture, use, offer for sale, sell or import our therapeutic candidates in the event of an infringement action.

In the event of patent infringement claims, or to avoid potential claims, we may choose or be required to seek a license from a third-party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be non-exclusive, which could potentially limit our competitive advantage. Ultimately, we could be prevented from commercializing a therapeutic candidate or be forced to cease some aspect of our business operations if, as a result of actual or threatened patent infringement or other claims, we are unable to enter into licenses on acceptable terms.

We may be unable to adequately protect or enforce our rights to intellectual property, causing us to lose valuable rights. Loss of any of our intellectual property rights may lead us to lose market share and could have an adverse effect on our business, results of operations and financial condition.

Our success depends, in part, on our ability, and the ability of our potential development and commercialization partners to obtain patent protection for our therapeutic candidates, maintain the confidentiality of our trade secrets and know-how, operate without infringing on the proprietary rights of others and prevent others from infringing our proprietary rights.

We try to protect our proprietary position by, among other things, filing U.S. and other patent applications related to our therapeutic candidates, inventions and improvements that may be important to the continuing development of our therapeutic candidates.

Because the patent position of pharmaceutical companies involves complex legal and factual questions, we cannot predict the validity and enforceability of any patents we may obtain with certainty. Our competitors may independently develop drug delivery technologies or products similar to ours or design around or otherwise circumvent any patents that may be issued to or licensed by us. Our pending patent applications, and those that we may file in the future or those we may license from third parties may not result in patents being issued. If these patents are issued, they may not provide us with proprietary protection or competitive advantages. The degree of future protection to be afforded by our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage.

Patent rights are territorial; thus, the patent protection we have sought will only extend, if issued, to those countries, if any, in which we will be issued patents. Even so, the laws of certain countries do not protect our intellectual property rights to the same extent as do the laws of the U.S. Competitors may successfully challenge any of our patents, produce similar drugs or products that do not infringe such patents, or produce drugs in countries where we have not applied for patent protection or that do not respect such patents. Furthermore, it is not possible to know the scope of claims that will be allowed in published applications and it is also not possible to know which claims of granted patents, if any, will be deemed enforceable in a court of law.

After the completion of development and registration of any future patents, third parties may still act to manufacture or market our therapeutic candidates in infringement of our patent protected rights. Such manufacture or marketing of our therapeutic candidates in infringement of any patent-protected rights is likely to cause us damage and lead to a reduction in the prices of our therapeutic candidates, thereby reducing our potential profits.

We may invest a significant amount of time and expense in the development of our therapeutic candidates only to be subject to significant delay and patent litigation before they may be commercialized. In addition, due to the extensive time needed to develop, test and obtain regulatory approval for our therapeutic candidates, any patents that may be issued that protect our therapeutic candidates may expire early during commercialization. This may reduce or eliminate any market advantages that such patents may give us. Following patent expiration, we may face increased competition through the entry of generic products into the market and a subsequent decline in market share and profits.

We are developing some of our therapeutic candidates in collaboration with academic and other research institutes and biopharmaceutical companies. While we attempt to ensure that our intellectual property is protected under the terms of our collaboration agreements with such institutes, these institutes may have claims to our intellectual property.

We do not have patent protection in certain countries, and we may not be able to effectively enforce our intellectual property rights in certain countries, which could significantly erode the market for our product candidates.

We intend to seek regulatory approval to market our oncology therapeutic candidates in a number of foreign countries. Our oncology therapeutic candidates are not protected by patents in certain countries, which means that competitors may be free to sell products that incorporate the same technology that is used in our products in those countries. In addition, the laws and practices in some foreign countries may not protect intellectual property rights to the same extent as in the United States. We or our licensors may not be able to effectively obtain, maintain or enforce rights with respect to the intellectual property relating to our oncology product candidates in those countries. In that regard, we believe that although China is one of the largest potential markets for some of our products under development, some of our product candidates are less protected by patents in China than in the U.S., and it may be difficult to enforce intellectual property rights in China. Our lack of patent protection in one or more countries, or the inability to obtain, maintain or enforce intellectual property rights in one or more countries, could adversely affect our ability to commercialize our products in those countries and could otherwise have a material adverse effect on our business.

If we are unable to protect the confidentiality of our trade secrets or know-how, such proprietary information may be used by others to compete against us.

In addition to filing patents, we generally try to protect our trade secrets, know-how and technology by entering into confidentiality or non-disclosure agreements with parties that have access to it, such as our current or potential development and commercialization partners, employees, contractors and consultants. We also enter into agreements that purport to require the disclosure and assignment to us of all, or certain, rights to the ideas, developments, discoveries and inventions of our employees, advisors, research collaborators, contractors and consultants while we employ or engage them. However, these agreements can be difficult and costly to enforce or may not provide adequate remedies. Any of these parties may breach the confidentiality agreements and willfully or unintentionally disclose our confidential information, or our competitors might learn of the information in some other way. The disclosure to, or independent development by, a competitor of any trade secret, know-how or other technology not protected by a patent could materially adversely affect any competitive advantage we may have over any such competitor. In addition, monitoring infringement of intellectual property rights is difficult, and we cannot be certain that the steps we have taken will prevent unauthorized use of our know-how, particularly in China and other countries in which the laws may not protect our proprietary rights as fully as the laws of the United States. Accordingly, other parties, including competitors, may improperly duplicate our products using our proprietary technologies. Pursuing legal remedies against persons infringing our patents or otherwise improperly using our proprietary information is a costly and time-consuming process that would divert management’s attention and other resources from the conduct of our normal business.

To the extent that any of our employees, advisors, research collaborators, contractors or consultants independently develop, or use independently developed, intellectual property in connection with any of our projects, disputes may arise as to the proprietary rights to this type of information. If a dispute arises with respect to any proprietary right, enforcement of our rights can be costly and unpredictable, and a court may determine that the right belongs to a third-party.

We may be subject to other patent-related litigation or proceedings that could be costly to defend and uncertain in their outcome.

In addition to infringement claims against us, we may in the future become a party to other patent litigation or proceedings before regulatory agencies, including interference or re-examination proceedings filed with the U.S. Patent and Trademark Office (USPTO) or opposition proceedings in other foreign patent offices regarding intellectual property rights with respect to our therapeutic candidates, as well as other disputes regarding intellectual property rights with our current and potential development and commercialization partners, or others with whom we have contractual or other business relationships. Post-issuance oppositions are not uncommon, and we and our current and potential development and commercialization partners will be required to defend these opposition procedures as a matter of course. Opposition procedures may be costly, and there is a risk that we may not prevail.

Risks Related to our Operations in Israel

We conduct our operations in Israel. Conditions in Israel, including the ongoing attacks by Hamas and other terrorist organizations from the Gaza Strip that were initiated in October 2023 and Israel's war against them, may affect our business, results of operations, and financial condition.

Because we are incorporated under the laws of the state of Israel and our operations are conducted in Israel, our business and operations are directly affected by economic, political, geopolitical and military conditions in Israel. Since the establishment of the State of Israel in 1948, a number of armed conflicts have occurred between Israel and its neighboring countries and terrorist organizations active in the region. These conflicts have involved missile strikes, hostile infiltrations and terrorism against civilian targets in various parts of Israel, which have negatively affected business conditions in Israel.

In October 2023, Hamas terrorists infiltrated Israel's southern border from the Gaza Strip and conducted a series of attacks on civilian and military targets. Hamas also launched extensive rocket attacks on Israeli population and industrial centers located along Israel's border with the Gaza Strip and in other areas within the State of Israel. Following the attack, Israel's security cabinet declared war against Hamas and a military campaign against these terrorist organizations commenced in parallel to their continued rocket and terror attacks. Moreover, the clash between Israel and Hezbollah in Lebanon, may escalate in the future into a greater regional conflict.

Any hostilities involving Israel, or the interruption or curtailment of trade within Israel or between Israel and its trading partners could adversely affect our operations and results of operations and could make it more difficult for us to raise capital. While five study sites out of 27 total study sites for the ongoing studies for CM24 and NT219 are located in Israel, we have not yet experienced any material interruptions or delays with respect to such studies, and we believe the study sites in Israel have sufficient supply of the therapeutic candidates to continue the studies, as applicable. Both CM24 and NT219 are manufactured by service providers outside of Israel. Most of our research and development work is being conducted by third-party entities outside of Israel. However, a prolonged conflict with Hamas may cause disruptions or delays to our study sites located in Israel, as a result of shortage of staff at such study sites, resulting in an adverse effect on our business, financial condition and results of operation.

Our commercial insurance does not cover losses that may occur as a result of events associated with the security situation in the Middle East. Although the Israeli government currently covers the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, we cannot assure you that this government coverage will be maintained or, if maintained, will be sufficient to compensate us fully for damages incurred. Any losses or damages incurred by us could have a material adverse effect on our business.

Parties with whom we may do business have sometimes declined to travel to Israel during periods of heightened unrest or tension, forcing us to make alternative arrangements when necessary. The conflict situation in Israel could cause situations where medical product certifying or auditing bodies could not be able to visit manufacturing facilities of our subcontractors in Israel in order to review our certifications or clearances, thus possibly leading to temporary suspensions or even cancellations of our product clearances or certifications. The conflict situation in Israel could also result in parties with whom we have agreements involving performance in Israel claiming that they are not obligated to perform their commitments under those agreements pursuant to force majeure provisions in such agreements.

There have been travel advisories imposed as related to travel to Israel, and restriction on travel, or delays and disruptions as related to imports and exports may be imposed in the future. An inability to receive supplies and materials, shortages of materials or difficulties in procuring our materials, among others, may adversely impact our ability to commercialize and manufacture our product candidates and products in a timely manner. This could cause a number of delays and/or issues for our operations, including delay of the review of our product candidates by regulatory agencies, which in turn would have a material adverse impact on our ability to commercialize our product candidates.

Additionally, all members of our management team and all of our employees are located and reside in Israel. Shelter-in-place and work-from-home measures, government-imposed restrictions on movement and travel and other precautions that may be taken to address the ongoing conflict may temporarily disrupt our management and employees' ability to effectively perform their daily tasks.

The Israel Defense Force (the "IDF"), the national military of Israel, is a conscripted military service, subject to certain exceptions. Several of our employees and management members are subject to military service in the IDF and have been and may be called to serve. There may be further or longer military reserve duty call-ups in the future, which may affect our business due to a shortage of skilled labor and loss of institutional knowledge, and necessary mitigation measures we may take to respond to a decrease in labor availability, such as overtime and third-party outsourcing, for example, which may have unintended negative effects and adversely impact our results of operations, liquidity or cash flows.

It is currently not possible to predict the duration or severity of the ongoing conflict or its effects on our business, operations and financial conditions. The ongoing conflict is rapidly evolving and developing, and could disrupt our business and operations, interrupt our sources and availability of supply and hamper our ability to raise additional funds or sell our securities, among others.

Any armed conflicts, terrorist activities or political instability in the region would likely negatively affect business conditions and could harm our results of operations and could make it more difficult for us to raise capital.

It may be difficult to enforce a U.S. judgment against us and our officers and directors in Israel or the U.S., to assert U.S. securities laws claims in Israel or to serve process on our officers and directors.

We are incorporated in Israel. Most of our executive officers and directors reside outside of the U.S., and all of our assets and most of the assets of our executive officers and directors are located outside of the U.S. Therefore, a judgment obtained against us or such executive officers and our directors in the U.S., including one based on the civil liability provisions of the U.S. federal securities laws, may not be collectible in the U.S. In addition, it may be difficult for you to affect service of process on these persons in the U.S. or to assert U.S. securities law claims in original actions instituted in Israel or obtain a judgment based on the civil liability provisions of U.S. federal securities laws. Israeli courts may refuse to hear a claim based on an alleged violation of U.S. securities laws against us or our non-U.S. officers and directors on the grounds that Israel is not the most appropriate forum to bring such a claim. In addition, even if an Israeli court agrees to hear a claim, it may determine that Israeli law and not United States law is applicable to the claim. If United States law is found to be applicable, the content of applicable United States law must be proven as a fact by expert witnesses, which can be a time consuming and costly process. Certain matters of procedure will also be governed by Israeli law. There is little binding case law in Israel that addresses the matters described above.

Additionally, Israeli courts might not enforce judgments obtained in the United States against us or our non-U.S. directors and executive officers, which may make it difficult to collect on judgments rendered against us or our non-U.S. officers and directors by either a U.S. or foreign court. Moreover, an Israeli court will not enforce a non-Israeli judgment if it was given in a state whose laws do not provide for the enforcement of judgments of Israeli courts (subject to exceptional cases), if its enforcement is likely to prejudice the sovereignty or security of the State of Israel, if it was obtained by fraud or in the absence of due process, if it is at variance with another valid judgment that was given in the same matter between the same parties, or if a suit in the same matter between the same parties was pending before a court or tribunal in Israel at the time the foreign action was brought.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful shareholder claims against us and may reduce the amount of money available to us.

The Companies Law and our amended and restated articles of association permit us to indemnify our directors and officers for acts performed by them in their capacity as directors and officers. The Companies Law and our amended and restated articles of association provide that a company may not exempt or indemnify a director or an office holder nor enter into an insurance contract, which would provide coverage for any monetary liability incurred as a result of (a) a breach by the director or officer of his duty of loyalty, except for insurance and indemnification where the director or officer acted in good faith and had a reasonable basis to believe that the act would not prejudice the company; (b) a breach by the director or officer of his duty of care if the breach was done intentionally or recklessly, except if the breach was solely as a result of negligence; (c) any act or omission done with the intent to derive an illegal personal benefit; or (d) any fine, civil fine, monetary sanctions, or forfeit imposed on the officer or director.

We have issued letters of indemnification to our directors and officers, pursuant to which we have agreed to indemnify them in advance for any liability or expense imposed on or incurred by them in connection with acts they perform in their capacity as a director or officer, to the fullest extent permitted by applicable law, to the extent that these liabilities are not covered by insurance. The total amount of the indemnity will not exceed 25% of our then consolidated shareholders' equity, per our most recent audited or reviewed consolidated financial statements.

Our indemnification obligations limit the personal liability of our directors and officers for monetary damages for breach of their duties as directors by shifting the burden of such losses and expenses to us. Although we have obtained directors' and officers' liability insurance, certain liabilities or expenses covered by our indemnification obligations may not be covered by such insurance or the coverage limitation amounts may be exceeded.

As a result of the class action motions and lawsuits, the Atzmon Claim described in "Item 8. Financial Information – A. Financial Statements and Other Financial Information – Legal Proceedings", or other claims which may be filed against our directors and officers, we may need to use a significant amount of our funds to satisfy our indemnification obligations, which could severely harm our business and financial condition and limit the funds available to shareholders who may choose to bring a claim against our company. See the risk factor titled "*Third-party claims of intellectual property infringement and other legal challenges may require us to spend substantial time and money and could prevent us from or delay us in developing or commercializing our therapeutic candidates. An adverse result in any infringement claims or other legal challenges could have a material adverse effect on our business, results of operations and on our financial condition*" under the risk factor section titled "Risks Related to Intellectual Property".

These provisions and resultant costs may also discourage us from bringing a lawsuit against directors and officers for breaches of their duties and may similarly discourage the filing of derivative litigation by our shareholders against the directors and officers even though such actions, if successful, might otherwise benefit our shareholders.

Provisions of Israeli law and our amended and restated articles of association may delay, prevent or otherwise impede a merger with, or an acquisition of the Company, or an acquisition of a significant portion of our shares, which could prevent a change of control, and negatively affect the market price of our ordinary shares.

Israeli corporate law regulates mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for certain transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to these types of transactions. These provisions of Israeli law may delay, prevent or make difficult an acquisition of us, which could prevent a change of control and therefore depress the price of our shares.

Furthermore, Israeli tax considerations may make potential transactions unappealing to us or to our shareholders, especially for those shareholders whose country of residence does not have a tax treaty with Israel which exempts such shareholders from Israeli tax. For example, Israeli tax law does not recognize tax-free share exchanges to the same extent as U.S. tax law. With respect to mergers, Israeli tax law allows for tax deferral in certain circumstances but makes the deferral contingent on the fulfillment of a number of conditions, including, in some cases, a holding period of two years from the date of the transaction during which sales and dispositions of shares of the participating companies are subject to certain restrictions. Moreover, with respect to certain share exchange transactions, the tax deferral is limited in time, and when such time expires, the tax becomes payable even if no disposition of the shares has occurred.

In addition, our amended and restated articles of association also contain provisions that could delay or prevent changes in control. These provisions include matters in connection with the election and removal of directors, such as our staggered Board, the right of our Board to appoint additional directors to fill vacancies on the Board, the size of our Board, the terms of office of our directors and the special majority required to amend such provision in our amended and restated articles of association.

Further, under our amended and restated articles of association, we have 50,000,000 shares of authorized non-voting senior preferred shares, which can be issued by our Board, which contain superior liquidation and dividend rights, and may contain other rights, including conversion, redemption, optional and other special rights, qualifications, limitations or restrictions, equivalent or superior to our ordinary shares, without further action by our shareholders, unless shareholder approval is otherwise required by applicable law, the rules of any exchange or other market on which our securities may then be listed or traded, our articles of association then in effect, or any other applicable rules and regulations. Furthermore, in a merger between Israeli companies, if the non-surviving entity has more than one class of shares, the merger may need to be approved by each class of shareholders, including any classes of otherwise non-voting shares, such as our authorized non-voting senior preferred shares. See *"We can issue non-voting senior preferred shares without shareholder approval, which could adversely affect the rights of holders of ordinary shares."*

These and other similar provisions could delay, prevent or impede an acquisition of us by a third-party or our merger with another company, or an acquisition of a significant portion of our shares, and may make it more difficult for our shareholders to elect different individuals to our Board, even if doing so would be considered to be beneficial by some of our shareholders, and may limit the price that investors may be willing to pay in the future for our ordinary shares.

Because a certain portion of our expenses is incurred in currencies other than the U.S. dollar, our results of operations may be harmed by currency fluctuations and inflation.

Our reporting and functional currency is the U.S. dollar. Most of the royalty payments from potential development and commercialization partners are expected to be payable in U.S. dollars, and we expect our revenues from future sales or licensing agreements to be denominated mainly in U.S. dollars. We pay a portion of our expenses in U.S. dollars; however, a portion of our expenses, related to salaries of our employees in Israel, our office lease and payment to part of the service providers in Israel, are paid in NIS and in other currencies, such as euro to our suppliers in Europe. In addition, a portion of our financial assets is held from time to time in NIS. As a result, we are exposed to currency fluctuation risks and inflation. For example, if the NIS appreciates against the U.S. dollar, our NIS expenses as reported in U.S. dollars may be higher than anticipated. In addition, if the NIS depreciates against the U.S. dollar, the U.S. dollar value of our financial assets held in NIS will decline.

Your rights and responsibilities as a shareholder are governed by Israeli law, which may differ in some respects from the rights and responsibilities of shareholders of U.S. companies. Israeli law may impose obligations and responsibilities on a shareholder of an Israeli company that are not imposed upon shareholders of corporations in the U.S.

We are incorporated under Israeli law. The rights and responsibilities of the holders of our ordinary shares are governed by our amended and restated articles of association and Israeli law. These rights and responsibilities differ in some respects from the rights and responsibilities of shareholders in typical U.S.-based corporations. In particular, a shareholder of an Israeli company has a duty to act in good faith and in a customary manner in exercising its rights and fulfilling its obligations toward the company and other shareholders and to refrain from abusing its power in the company, including, among other things, in voting at the general meeting of shareholders on matters such as amendments to a company's articles of association, increases in a company's authorized share capital, mergers and acquisitions and related party transactions requiring shareholder approval under the Companies Law. In addition, a controlling shareholder of an Israeli company or a shareholder who knows that it possesses the power to determine the outcome of a shareholder vote or who has the power to appoint or prevent the appointment of a director or executive officer in the company or has other powers toward the company has a duty of fairness toward the company. There is limited case law available to assist us in understanding the implications of these provisions that govern shareholders' actions. These provisions may be interpreted to impose additional obligations and responsibilities on holders of our ordinary shares and/or ADSs that are not typically imposed on shareholders of U.S. corporations.

Our amended and restated articles of association designate courts located either within the State of Israel, or the Federal District Courts of the United States, as the exclusive forum for certain litigation that may be initiated by our shareholders, which could limit our shareholders' ability to bring a favorable or convenient judicial forum for disputes with us.

Our amended and restated articles of association provide that, unless we consent in writing to the selection of an alternative forum, the Tel Aviv District Court (Economic Division in the State of Israel (or, if the Tel Aviv District Court does not have jurisdiction, and no other Israeli court has jurisdiction, the federal district court for the District of New York) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our shareholders, and (3) any action asserting a claim arising pursuant to any provision of the Companies Law or the Israeli Securities Law 5728-1968, in all cases subject to the court's having personal jurisdiction over the indispensable parties named as defendants. In addition, other than with respect to plaintiffs or a class of plaintiffs which may be entitled to assert a cause of action arising under the Securities Act of 1933 in the courts of the State of Israel, the federal district courts of the United States for the District of New York shall otherwise be the exclusive forum for any complaint asserting a cause of action arising under the Securities Act of 1933. Any person or entity purchasing or otherwise acquiring any interest in our shares or ADSs shall be deemed to have notice of and consented to these provisions. This forum selection provision limits shareholders' choice in selecting a judicial forum for disputes with us that it finds favorable or convenient and may have the effect of discouraging lawsuits against us or our directors and officers.

Risks Primarily Related to Our ADSs and Ordinary Shares

The market price of our ordinary shares and ADSs is subject to fluctuation, which could result in substantial losses by investors.

The stock market in general, and the market price of our ordinary shares on the TASE and ADSs on NASDAQ, are subject to fluctuation, and changes in the price of our listed securities may be unrelated to our operating performance. The market prices of our ordinary shares on the TASE and ADSs on NASDAQ have fluctuated in the past, and we expect it will continue to do so. The market price of our ordinary shares and ADSs is and will be subject to a number of factors, including:

- announcements of technological innovations or new therapeutic candidates by us or by others;
- announcements by us of significant acquisitions, strategic partnerships, in-licensing, out-licensing, joint ventures or capital commitments;

- announcement by us of preclinical and clinical results;
- our need to raise additional capital;
- expiration or terminations of licenses, research contracts or other development or commercialization agreements;
- public concern as to the safety of drugs that we, our current or potential development and commercialization partners or others develop;
- the volatility of market prices for shares of biotechnology companies generally;
- success or failure of research and development projects;
- departure of key personnel;
- developments concerning intellectual property rights or regulatory approvals;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts;
- the outcome of any litigation and other legal proceedings;
- changes in government regulations or patent decisions;
- developments by our current or potential development and commercialization partners; and
- general economic and market conditions and other factors, including factors unrelated to our operating performance and including the impact of Israel's war with Hamas and other militant groups and the ongoing effects of the COVID-19 endemic.

These factors and any corresponding price fluctuations may materially and adversely affect the market price of our ordinary shares and ADSs and result in substantial losses by investors.

Additionally, market prices for listed securities of biotechnology and pharmaceutical companies have been very volatile and have experienced significant price and volume fluctuations for reasons often unrelated to the operating performance of any one company. These fluctuations may be attributed, among other reasons, to the COVID-19 endemic or more recently to general global economic environment and the instability in markets. In the past, following periods of market volatility, shareholders have often instituted securities class action litigation. If we were involved in securities litigation, it could have a substantial cost and divert resources and attention of management from our business, even if we are successful. See "*Third-party claims of intellectual property infringement and other legal challenges may require us to spend substantial time and money and could prevent us from or delay us in developing or commercializing our therapeutic candidates. An adverse result in any infringement claims or other legal challenges could have a material adverse effect on our business, results of operations and on our financial condition*."

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, on our business, results of operations and financial condition, and on the market price ADSs or ordinary shares.

Future sales of our ordinary shares or ADSs, or securities convertible into our ordinary shares or ADSs, or the perception that future sales may occur, could reduce the market price of our ordinary shares and ADSs.

As of March 5, 2024, we had an aggregate of 265,584,738 issued and outstanding ordinary shares (including 1 dormant ordinary share held in treasury), no non-voting senior preferred shares, outstanding non-listed warrants to purchase 8,342,532 ADSs (representing 83,425,320 ordinary shares) issued to investors, underwriters and placement agents as part of a number of public and registered direct offerings by us and 24,962,206 outstanding options and restricted share units ("RSUs"). In the future, we may issue additional ordinary shares, ADSs or other equity or debt securities exercisable or convertible into ordinary shares or ADSs.

On June 9, 2021, we entered into the Sales Agreement with Jefferies for the sale of ADSs, pursuant to which we may offer and sell ADSs from time to time under our ATM program, with Jefferies acting as our agent. We originally filed a prospectus for a $50.0 million ATM program, but the aggregate offering price was subsequently reduced to $21.0 million on March 23, 2022, and to $3.0 million on October 17, 2023. As of March 5, 2024, we have sold approximately 2,217,325 of our ADSs for total gross proceeds of $4.0 million under the Sales Agreement.

On December 8, 2022, we filed a registration statement on Form F-3 with the SEC utilizing a "shelf" registration process, under which we may offer and sell, from time to time in one or more offerings, up to an aggregate $200,000,000 of ADSs (representing our ordinary shares), ordinary shares, preferred shares, warrants, overallotment purchase rights, subscription rights, units and/or capital notes. In October 2023, we completed a $5 million registered direct offering with an institutional investor for the purchase and sale of 2,430,000 ADSs and pre-funded warrants to purchase up to 1,917,827 ADS, and, in a concurrent private placement, unregistered warrants to purchase up to 4,347,827 ADSs, which are exercisable immediately. In November 2023, we filed a registration statement on Form F-1 with the SEC, under which the investor and placement agent in the offering may resell from time to time the ADSs issuable upon exercise of the unregistered warrants issued to them in the offering. If these registered ADSs issuable upon exercise of the unregistered warrants are sold to the public, the market price of our ADSs may decline.

Any future sales by us or our shareholders of a substantial number of our ordinary shares or ADSs, or securities convertible into our ordinary shares or ADSs, or the perception that such sales may occur in the future, including sales of ordinary shares or ADSs issuable upon the exercise of warrants or options, the vesting or RSUs or the conversion of convertible securities, may cause the market price of our ordinary shares or ADSs or other listed securities to decline.

We may not meet the continued listing requirements of NASDAQ, which could result in a delisting of the ADSs from NASDAQ.

The ADSs are listed on NASDAQ. We have in the past, and may in the future, be unable to comply with certain of the listing standards that we are required to meet to maintain the listing of ADSs on NASDAQ.

On January 25, 2024, we received a letter from the Listings Qualifications Department of The Nasdaq Stock Market LLC indicating that, based on the closing bid price of the ADSs for the last 30 consecutive business days, from December 11, 2023, to January 24, 2024, we did not meet the minimum bid price of $1.00 per share required for continued listing on NASDAQ pursuant to NASDAQ Listing Rule 5550(a)(2). In accordance with NASDAQ Listing Rule 5810(c)(3)(A), we have an initial period of 180 calendar days from the date of the notification letter from The Nasdaq Stock Market LLC, or until July 23, 2024, to regain compliance with the minimum bid price requirement. If at any time before July 23, 2024, the closing bid price of the ADSs is at least $1.00 for a minimum of ten consecutive business days, The Nasdaq Stock Market LLC will provide a written confirmation of compliance and the matter will be closed. In the event we do not regain compliance by July 23, 2024, we may then be eligible for an additional 180 calendar day period to regain compliance. To qualify, we will be required to meet the continued listing requirement for market value of publicly held shares and all other initial listing standards for NASDAQ, with the exception of the bid price requirement, and will need to provide written notice of our intention to cure the deficiency during the second compliance period, by effecting a change in the ratio between the ADSs and our ordinary shares, if necessary. However, if it appears to The Nasdaq Stock Market LLC staff that we will not be able to cure the deficiency during the second compliance period, or if we are not otherwise eligible, The Nasdaq Stock Market LLC will provide written notice that the ADSs are subject to delisting from NASDAQ. In that event, we may appeal the determination to a Nasdaq Stock Market LLC hearings panel. If we fail to regain compliance within our applicable cure period, or fail to satisfy other listing requirements, the ADSs may be subject to delisting.

We intend to monitor the closing bid price of the ADSs and may, if appropriate, consider implementing available options to cure the deficiency and regain compliance with the NASDAQ minimum bid price requirement within the compliance period. However, we can provide no assurance that any action taken by us would be successful, or that any such action would stabilize the market price or improve the liquidity of the ADSs.

If NASDAQ delists the ADSs from trading on its exchange for failure to meet the listing standards, an investor would likely find it significantly more difficult to dispose of or obtain ADSs, and our ability to raise future capital through the sale of ADSs could be severely limited. We additionally may not be able to list ADSs on another national securities exchange, which could result in our securities being quoted on an over-the-counter market. If this were to occur, our shareholders could face significant material adverse consequences, including limited availability of market quotations for ADSs and reduced liquidity for the trading of our securities. In addition, we could experience a decreased ability to issue additional securities and obtain additional financing in the future. There can be no assurance that an active trading market for ADSs will develop or be sustained. As a result of these factors, if the ADSs are delisted from NASDAQ, the price of our ADSs is likely to decline. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities.

If our ADSs are delisted from NASDAQ, we would remain a publicly traded company on the TASE and revert to being subject to full Israeli securities laws and disclosure requirements. Accordingly, we will need to comply with U.S. and Israeli disclosure requirements, and we expect that these additional reporting requirements would increase our legal and financial compliance costs and require significant management time.

In the event that our ADSs are delisted from NASDAQ, U.S. broker-dealers may be discouraged from effecting transactions in our ADSs because they may be considered penny stocks and thus be subject to the penny stock rules.

The SEC has adopted a number of rules to regulate “penny stock” that restrict transactions involving stock which is deemed to be penny stock. Such rules include Rules 3a51-1, 15g-1, 15g-2, 15g-3, 15g-4, 15g-5, 15g-6, 15g-7, and 15g-9 under the Securities and Exchange Act of 1934, as amended (the “Exchange Act”). These rules may have the effect of reducing the liquidity of penny stocks. “Penny stocks” generally are equity securities with a price of less than $5.00 per share (other than securities registered on certain national securities exchanges or quoted on NASDAQ if current price and volume information with respect to transactions in such securities is provided by the exchange or system). Following a delisting from NASDAQ, our ADSs may constitute “penny stock” within the meaning of these rules. The additional sales practice and disclosure requirements imposed upon U.S. broker-dealers may discourage such broker-dealers from effecting transactions involving our ADSs, which could severely limit the market liquidity of the ADSs and impede their sale in the secondary market.

A U.S. broker-dealer selling penny stock to anyone other than an established customer or “accredited investor” (generally, an individual with net worth in excess of $1,000,000 or an annual income exceeding $200,000, or $300,000 together with his or her spouse) must make a special suitability determination for the purchaser and must receive the purchaser’s written consent to the transaction prior to sale, unless the broker-dealer or the transaction is otherwise exempt. In addition, the “penny stock” regulations require the U.S. broker-dealer to deliver, prior to any transaction involving a “penny stock”, a disclosure schedule prepared in accordance with SEC standards relating to the “penny stock” market, unless the broker-dealer or the transaction is otherwise exempt. A U.S. broker-dealer is also required to disclose commissions payable to the U.S. broker-dealer and the registered representative and current quotations for the securities. Finally, a U.S. broker-dealer is required to submit monthly statements disclosing recent price information with respect to the “penny stock” held in a customer’s account and information with respect to the limited market in “penny stocks”.

Securities holders should be aware that, according to the SEC, the market for “penny stocks” has suffered in recent years from patterns of fraud and abuse. Such patterns include (i) control of the market for the security by one or a few broker-dealers that are often related to the promoter or issuer; (ii) manipulation of prices through prearranged matching of purchases and sales and false and misleading press releases; (iii) “boiler room” practices involving high-pressure sales tactics and unrealistic price projections by inexperienced sales persons; (iv) excessive and undisclosed bid-ask differentials and markups by selling broker-dealers; and (v) the wholesale dumping of the same securities by promoters and broker-dealers after prices have been manipulated to a desired level, resulting in investor losses.

We incur increased costs and risks as a result of operating as a public company in the U.S. and Israel, and our management is and will continue to be required to devote substantial time to compliance initiatives.

Our ADSs have been traded on NASDAQ since November 20, 2015, and prior to that our ordinary shares traded on the TASE, where they continue to trade. As a public company whose securities are listed in the United States and Israel, we incur accounting, legal and other expenses, including costs associated with our reporting requirements under the Exchange Act and the Israeli Securities Law. We also incur costs associated with corporate governance requirements, including requirements under Section 404 and other provisions of the Sarbanes-Oxley Act, as well as rules implemented by the SEC and NASDAQ, and provisions of Israeli corporate and securities laws applicable to public companies. Certain aspects of Israeli securities laws are different than U.S. securities law, and our dual listing on TASE exposes us and our management to differing regulatory regimes which may involve increased regulatory risk.

Pursuant to Section 404 of the Sarbanes-Oxley Act and the related rules adopted by the SEC and the Public Company Accounting Oversight Board, our management is required to report on the effectiveness of our internal control over financial reporting. In addition, if we become an “accelerated filer” or a “large accelerated filer” as those terms are defined under Rule 12b-2 of the Exchange Act, our independent registered public accounting firm will be required to attest to our evaluation of internal controls over financial reporting. Unless we successfully design and implement changes to our internal controls and management systems, or if we fail to maintain the adequacy of these controls as such standards are modified or amended from time to time, we may not be able to comply with Section 404. As a result, our auditors may be unable to attest to the effectiveness of our internal controls over financial reporting. This could subject us to regulatory scrutiny and result in a loss of public confidence in our management, which could, among other things, adversely affect the price of our ordinary shares and our ability to raise additional capital.

The process of determining whether our existing internal controls over financial reporting systems are compliant with Section 404 and whether there are any material weaknesses or significant deficiencies in our existing internal controls, requires the investment of substantial time and resources, including by our chief executive officer, chief financial officer and other members of our senior management. As a result, this process may divert internal resources and take a significant amount of time and effort to complete.

We cannot predict the outcome of evaluations we will conduct in the future, and whether we will need to implement additional remedial actions in order to implement effective controls over financial reporting. The determination and any remedial actions required could result in us incurring additional costs that we did not anticipate, including the hiring of outside consultants. Irrespective of compliance with Section 404, any failure of our internal controls could have a material adverse effect on our stated results of operations and harm our reputation. As a result, we may experience higher than anticipated operating expenses, as well as higher independent auditor fees during and after the implementation of these changes. If we are unable to implement any of the required changes to our internal control over financial reporting effectively or efficiently, it could adversely affect our operations, financial reporting and/or results of operations and could result in an adverse opinion on internal controls from our independent auditors and cause the market price of our ordinary shares and ADSs to decline.

Changes in the laws and regulations affecting public companies may result in increased costs to us as we respond to their requirements. These laws and regulations could make it more difficult or costlier for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our Board, our board committees or as executive officers. We cannot predict or estimate the amount or timing of additional costs we may incur in order to comply with such requirements.

We are a non-accelerated filer, and we cannot be certain if the reduced disclosure requirements applicable to us will make our ADSs less attractive to investors.

We are currently a "non-accelerated filer", as those terms are defined in the Securities Act. Accordingly, we take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not a "non-accelerated filers," in particular, reduced disclosure obligations regarding exemptions from the provisions of Section 404(b) of the Sarbanes-Oxley Act of 2002 requiring that independent registered public accounting firms provide an attestation report on the effectiveness of internal control over financial reporting. Decreased disclosures in our SEC filings due to our status as a "non-accelerated filer" may make it harder for investors to analyze our results of operations and financial prospects.

We cannot predict if investors will find our ADSs less attractive if we rely on exemptions applicable to smaller reporting companies and non-accelerated filers. If some investors find our ADSs less attractive as a result, there may be a less active trading market for our ADSs and our ordinary share price may be more volatile.

We may be classified as a Passive Foreign Investment Company, or PFIC, for U.S. federal income tax purposes in 2023 and may continue to be, or become, a PFIC in future years, which may have negative tax consequences for U.S. investors.

We will be treated as a PFIC for U.S. federal income tax purposes in any taxable year in which either (i) at least 75% of our gross income is "passive income" or (ii) on average at least 50% of our assets by value produce passive income or are held for the production of passive income. Based on our estimated gross income, the average value of our gross assets, and the nature of our business, we believe it is likely that we were a PFIC in 2023 and we may also be classified as a PFIC in future years. If we are treated as a PFIC for any taxable year during which a U.S. investor held our ADSs, certain adverse U.S. federal income tax consequences could apply to the U.S. investor.

As a foreign private issuer, we are permitted to follow certain home country corporate governance practices instead of applicable NASDAQ requirements, which may result in less protection than is accorded to investors under rules applicable to U.S. domestic issuers.

As a foreign private issuer, we are permitted to follow certain home country corporate governance practices instead of those otherwise required under the NASDAQ Listing Rules for U.S. domestic issuers. We follow home country practice in Israel with regard to (among other things) director nomination procedures, quorum requirement at shareholder meetings and approval of related party transactions and executive compensation. In addition, we follow our home country law, instead of the NASDAQ Listing Rules, which require that we obtain shareholder approval for certain dilutive events, such as for the establishment or amendment of certain equity-based compensation plans, an issuance that will result in a change of control of the company, certain transactions other than a public offering involving issuances of a 20% or more interest in the Company and certain acquisitions of the stock or assets of another company. In the future we may elect to follow additional home country corporate governance practices instead of those otherwise required under the NASDAQ Listing Rules for U.S. domestic issuers. Following our home country governance practices as opposed to the requirements that would otherwise apply to a U.S. company listed on NASDAQ may provide less protection than is accorded to investors under the NASDAQ Listing Rules applicable to domestic issuers. See "Item 16G. Corporate Governance."

We are a "foreign private issuer" and have disclosure obligations that are different from those of U.S. domestic reporting companies. As a result, we may not provide you the same information as U.S. domestic reporting companies or we may provide information at different times, which may make it more difficult for you to evaluate our performance and prospects.

We are a foreign private issuer and, as a result, are not subject to the same requirements as U.S. domestic issuers. Under the Exchange Act, we are subject to reporting obligations that, in certain respects, are less detailed and/or less frequent than those of U.S. domestic reporting companies. For example, as a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act, related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as domestic companies whose securities are registered under the Exchange Act.

We intend to file with the SEC, within 120 days after the end of each fiscal year ending December 31, an annual report on Form 20-F containing financial statements which will be examined and reported on, with an opinion expressed, by an independent registered public accounting firm. In accordance with NASDAQ Listing Rules, as a foreign private issuer we are required to submit on a Form 6-K an interim balance sheet and income statement as of the end of the second quarter of each fiscal year. We have also agreed contractually under the Sales Agreement to provide an interim balance sheet and income statement as of the end of the first and third quarters of each fiscal year.

Foreign private issuers are also exempt from Regulation FD, which is intended to prevent issuers from making selective disclosures of material information. As a result of all of the above, you may not have the same protections afforded to shareholders of a company that is not a foreign private issuer.

We may lose our foreign private issuer status in the future, which could result in significant additional costs and expenses.

As discussed above, we are a foreign private issuer, and therefore, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act. The determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter, and, accordingly, the next determination will be made with respect to us on June 30, 2024. In the future, we would lose our foreign private issuer status if (1) more than 50% of our outstanding voting securities continue to be owned by U.S. residents and (2) a majority of our directors or executive officers are U.S. citizens or residents, or we fail to meet additional requirements necessary to avoid loss of foreign private issuer status. If we lose our foreign private issuer status, we will be required to file with the SEC periodic reports and registration statements on U.S. domestic issuer forms, which are more detailed and extensive than the forms available to a foreign private issuer. We will also have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors and principal shareholders will become subject to the short-swing profit disclosure and recovery provisions of Section 16 of the Exchange Act. In addition, we will lose our ability to rely upon exemptions from certain corporate governance requirements under the NASDAQ Listing Rules. As a U.S. listed public company that is not a foreign private issuer, we will incur significant additional legal, accounting and other expenses that we do not incur as a foreign private issuer.

The ADS holders may not be able to fully exercise their voting rights to the same extent as our ordinary shareholders. The depositary for the ADSs will give us a discretionary proxy to vote our ordinary shares underlying ADSs if a holder of the ADSs does not provide voting instructions, except in limited circumstances, which could adversely affect their interests.

The ADS holders may instruct the depositary how to vote the number of deposited ordinary shares their ADSs represent. Except by instructing the depositary, you will not be able to exercise voting rights unless you surrender your ADSs and withdraw the shares. However, you may not know about the meeting enough in advance to withdraw the shares. We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote your shares. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. This means that you may not be able to exercise voting rights and there may be nothing you can do if your shares are not voted as you requested, and you cannot vote in person at meetings as a holder of ADSs.

Under the deposit agreement for the ADSs, the depositary will give us a discretionary proxy to vote our ordinary shares underlying ADSs at shareholders' meetings if a holder of the ADSs does not provide voting instructions, unless we notify the depositary that:

- we do not wish to receive a discretionary proxy;
- there is substantial shareholder opposition to the particular question; or
- the particular question would have an adverse impact on our shareholders' rights.

The effect of this discretionary proxy is that a holder of the ADSs cannot prevent our ordinary shares underlying such ADSs from being voted, absent the situations described above, and it may make it more difficult for shareholders to influence the management of our company. Holders of our ordinary shares listed for trading on the TASE are not subject to this discretionary proxy.

We currently do not anticipate paying cash dividends, and accordingly, shareholders must rely on the appreciation in our ordinary shares and ADSs for any return on their investment.

We currently anticipate that we will retain future earnings, if any, for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. The ability of an Israeli company to pay dividends or repurchase its shares is governed by Israeli law, which provides that unless otherwise approved by a court, distributions, including cash dividends and share repurchases, may be made only out of retained earnings as determined for statutory purposes, and only if there is no reasonable concern that the dividend distribution will prevent us from meeting our existing and foreseeable obligations, as they become due. Subject to the foregoing, payment of future dividends, if any, will be at the discretion of our Board and will depend on various factors, such as our financial condition, operating results, current and anticipated cash needs and other business and economic factors that our Board may deem relevant. Since we do not have earnings, we currently do not have any ability to pay dividends or repurchase our shares, absent court approval. Therefore, the success of an investment in our ordinary shares and ADSs will depend upon any future appreciation in their value. There is no guarantee that our ordinary shares and ADSs will appreciate in value or even maintain the price at which our holders have purchased their shares and ADSs.

Investors in the ADSs may not receive the same distributions or dividends as those we make to the holders of our ordinary shares, and, in some limited circumstances, investors in the ADSs may not receive any value for them, if it is illegal or impractical to make them available to investors in the ADSs.

The depositary for the ADSs has agreed to pay investors in the ADSs the cash dividends or other distributions it or the custodian receives on ordinary shares or other deposited securities underlying the ADSs, after deducting its fees and expenses. Investors in our ADSs will receive these distributions in proportion to the number of ordinary shares their ADSs represent. However, the depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any holders of ADSs. For example, it would be unlawful to make a distribution to a holder of ADSs if it consists of securities that require registration under the Securities Act of 1933, as amended, or the Securities Act, but that are not properly registered or distributed under an applicable exemption from registration. In addition, conversion into U.S. dollars from foreign currency that was part of a dividend which was distributed in foreign currency made in respect of deposited ordinary shares may require the approval or license of, or a filing with, any government or agency thereof, which may be unobtainable. In these cases, the depositary may determine not to distribute such property and hold it as “deposited securities” or may seek to affect a substitute dividend or distribution, including net cash proceeds from the sale of the dividends that the depositary deems an equitable and practicable substitute. We have no obligation to register under U.S. securities laws any ADSs, ordinary shares, rights or other securities received through such distributions. We also have no obligation to take any other action to permit the distribution of ADSs, ordinary shares, rights or anything else to holders of ADSs. In addition, the depositary may withhold from such dividends or distributions its fees and an amount on account of taxes or other governmental charges to the extent the depositary believes it is required to make such withholding. This means that investors in our ADSs may not receive the same distributions or dividends as those we make to the holders of our ordinary shares, and, in some limited circumstances, investors in the ADSs may not receive any value for such distributions or dividends if it is illegal or impractical for us to make them available to investors in the ADSs. These restrictions may cause a material decline in the value of the ADSs.

Holders of ADSs must act through the depositary to exercise rights of shareholders of our company.

Holders of the ADSs do not have the same rights as our shareholders and may only exercise the voting rights with respect to the underlying ordinary shares in accordance with the provisions of the deposit agreement for the ADSs. Under Israeli law, the minimum notice period required to convene a shareholders’ meeting is no less than 35 or 21 calendar days, depending on the proposals on the agenda for the shareholders’ meeting. When a shareholder meeting is convened, holders of the ADSs may not receive sufficient notice of the meeting to permit them to withdraw their ordinary shares to allow them to cast their vote with respect to any specific matter. In addition, the depositary and its agents may not be able to send notice to holders of the ADSs or carry out their voting instructions in a timely manner. We will make all reasonable efforts to cause the depositary to extend voting rights to holders of the ADSs in a timely manner, but we cannot assure holders that they will receive the voting materials in time to ensure that they can instruct the depositary to vote the ordinary shares underlying their ADSs. Furthermore, the depositary and its agents will not be responsible for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, holders of the ADSs may not be able to exercise their right to vote and they may lack recourse if the ordinary shares underlying their ADSs are not voted as they requested. In addition, ADS holders will not be able to call a shareholders’ meeting unless they first withdraw their ordinary shares from the ADS program and receive delivery of the underlying ordinary shares held in the Israeli market in order to allow them to submit to us a request to call a meeting with respect to any specific matter, in accordance with the applicable provisions of the Companies Law and our amended and restated articles of association.

Our ordinary shares and our ADSs are traded on different markets and this may result in price variations.

Our ordinary shares trade on the TASE, and the ADSs trade on NASDAQ. Trading on these markets take place in different currencies (U.S. dollars on NASDAQ and NIS on the TASE), and at different times (resulting from different time zones, different trading days and different public holidays in the U.S. and Israel). The trading prices of our securities on these two markets may differ due to these and other factors. Any decrease in the price of our securities on one of these markets could cause a decrease in the trading price of our securities on the other market.

The ADSs have relatively limited trading volume, which may limit the ability of our investors to sell their ADSs in the U.S.

The ADSs have been traded at low volumes in the past and may be traded at low volumes in the future for reasons related or unrelated to our performance. This low trading volume may result in lesser liquidity and lower than expected market prices for ADSs, and our investors may not be able to resell their ADSs for more than they paid for them.

We can issue non-voting senior preferred shares without shareholder approval, which could adversely affect the rights of holders of ordinary shares.

Our amended and restated articles of association permit us to establish the rights, privileges, preferences and restrictions of future series of our non-voting senior preferred shares, which contain superior liquidation and dividend rights, and may contain other rights, including conversion, redemption, optional and other special rights, qualifications, limitations or restrictions, equivalent or superior to our ordinary shares and to issue such non-voting senior preferred shares without further approval from our shareholders. The rights of holders of our ordinary shares and ADSs may suffer as a result of the rights granted to holders of non-voting senior preferred shares that we may issue in the future. In addition, we could issue non-voting senior preferred shares containing rights that prevent a change in control or merger, thereby depriving holders of our ordinary shares and ADSs of an opportunity to sell their shares at a price in excess of the prevailing market price.

If equity research analysts do not publish research or reports about our business or if they issue unfavorable commentary or downgrade our ordinary shares or ADSs, the price of our ordinary shares and ADSs could decline.

The trading market for our ordinary shares and ADSs will rely in part on the research and reports that equity research analysts publish about us and our business. The price of our ordinary shares and ADSs could decline if such research or reports are not published or if one or more securities analysts downgrade the ADSs or if those analysts issue other unfavorable commentary or cease publishing reports about us or our business.

We have broad discretion as to the use of the net proceeds from our previous offerings and may not use them effectively.

We currently intend to use the net proceeds from our previous offerings, including under our ATM program, to expand our clinical development program, expand our clinical development pipeline for additional drug products, including by way of possible acquisitions, expand our pre-clinical development activity and for general corporate purposes, including working capital requirements. However, our management will have broad discretion in the application of the net proceeds from our previous offerings. Our shareholders may not agree with the manner in which our management chooses to allocate the net proceeds from our previous offerings. The failure by our management to apply these funds effectively could have a material adverse effect on our business, financial condition and results of operations. Pending their use, we may invest the net proceeds from our previous offerings in a manner that does not produce income. The decisions made by our management may not result in positive returns on any investment by shareholders and shareholders will not have an opportunity to evaluate the economic, financial or other information upon which our management bases its decisions.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

We were incorporated under the laws of the State of Israel (under a previous name) on August 12, 1968. Our ordinary shares were originally listed for trading on the TASE in 1978 and our ADSs have been traded on NASDAQ since November 2015. Our ordinary shares are currently traded on the TASE under the symbol "PPBT", and our ADSs are currently traded on NASDAQ under the symbol "PPBT". The Company is headquartered in Rehovot, Israel and our telephone number is +972-3-933-3121. Our website address is www.purple-biotech.com. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report and is not incorporated by reference herein. We have included our website address in this Annual Report solely for informational purposes. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers, such as us, that file electronically with the SEC at www.sec.gov.

In October 2012, the District Court in Lod, Israel approved the creditors arrangement in accordance with Section 350 of the Companies Law in order to effectuate the sale by our company (then known as Mainrom Line Logistics Ltd.) of all its activities, assets, rights, obligations and liabilities to a private company held by its then controlling shareholders, and all rights of our creditors against us were extinguished. From the completion of these transactions until the completion of the acquisition of Kitov Pharmaceuticals described below, Purple Biotech (then known as Kitov Pharma) did not conduct any business activities and was a public shell company listed on the TASE with no assets, debt and/or liabilities.

On July 11, 2013, we acquired Kitov Pharmaceuticals, which, prior to the completion of its merger with and into our company in December 2017, together with our company, was engaged in the research and development of Consensi. As part of the acquisition, Mainrom Line Logistics Ltd. changed its name to Kitov Pharmaceuticals Holdings Ltd., which name was subsequently changed in January 2018 to Kitov Pharma Ltd.

On January 13, 2017, we announced that we had acquired a majority equity stake in TyrNovo, a privately held developer of novel small molecules in the oncology therapeutic field.

On April 25, 2017, the boards of directors of each of Kitov Pharma and Kitov Pharmaceuticals approved a merger between the two entities, with Kitov Pharma remaining as the surviving entity. The merger was completed in December 2017. Kitov Pharmaceuticals was dissolved upon the merger, and Kitov Pharma remained as the surviving entity.

In January 2020, we completed the acquisition of FameWave, a privately held biopharmaceutical company, whose main asset is CM24, a clinical stage humanized monoclonal antibody in the oncology therapeutic field.

On December 7, 2020, we changed our name to Purple Biotech Ltd.

In December 2021, we decided to discontinue the manufacturing and distribution of Consensi.

In February 2023, we completed the acquisition of Immunorizon, a privately held biotech company developing multi-specific antibodies as oncology therapies that selectively activate the immune response within the TME. For information regarding the Immunorizon acquisition, see "Item 10 – Additional Information – C. Material Contracts – Immunorizon Acquisition."

For a description of our principal capital expenditures for the three years ended December 31, 2023, see "Item 5. *Operating and Financial Review and Prospects*."