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 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 pharmaceutical company, and we are focused on the development and commercialization of innovative pharmaceutical drugs. We have one FDA-approved drug, Consensi for which we have entered into commercialization agreements with respect to the United States and in several territories in Asia (subject to regulatory approval in such territories). We commenced commercial sales of Consensi in the United States in May 2020 but have not commenced drug sales in any other territory. Additionally, we currently have two oncology therapeutic candidates, NT219 and CM24, neither of which has been approved for marketing and they are not being sold, marketed or commercialized. 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 NT219, CM24 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, 2020 of approximately $$77.5 million as a result of 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 or other therapeutic candidates that we may develop 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 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; to successfully market and sell our FDA-approved drug Consensi in the United States through our U.S. commercialization partner; and to obtain, either by us or by our commercialization partners, the required regulatory approvals in various territories other than the United States and then commercialize and sell Consensi in such other territories. We may be unable to achieve any or all of these goals with regard to NT219, CM24 or any other therapeutic candidates that we may develop in the future and our FDA-approved drug Consensi. 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 products for our 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, gaining regulatory approval, and commercializing Consensi; developing our NT219 and CM24 therapeutic candidates; research and development; raising capital; and recruiting scientific and management personnel and third party partners. Though we have plans for the development and acquisition of additional therapeutic candidate products, to date the only revenue we have received has been the initial milestone payments in connection with commercialization agreements for Consensi. We have not yet demonstrated an ability to successfully generate significant revenues from Consensi. We have also not yet demonstrated an ability to commercialize or obtain regulatory approval for our NT219 and CM24 therapeutic candidates. Our future growth and success depend upon the successful commercialization of Consensi and our oncology therapeutic candidates. If we are unable to achieve increased commercial acceptance of our products or obtain regulatory clearances or approvals for our therapeutic candidates and future products, or if we experience a decrease in the utilization of our products, our revenue 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 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, as well as to acquire 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 therapeutic candidates, seek regulatory approval that is a prerequisite to selling any product, attract development or commercial partners and retain key personnel.***

Our business presently generates limited revenues, and we plan to continue expending substantial funds in research and development, including CMC, preclinical and clinical trials of our NT219 and CM24 therapeutic candidates, and for manufacturing of our FDA-approved drug Consensi, as well as to acquire or in-license additional therapeutic candidates. We plan to fund our future operations through commercialization and out-licensing of our products and therapeutic candidates and by 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. Moreover, to the extent we are able to raise capital through the issuance of debt or equity securities, it could result in substantial dilution to existing shareholders.

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 and our FDA-approved drug Consensi, we will need to raise substantial additional funds to develop and/or commercialize our therapeutic candidates and to 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 or develop in the future;
- our ability to successfully commercialize our oncology therapeutic candidates, or any other therapeutic candidates that we may acquire or develop in the future, including securing commercialization agreements with third parties and favorable pricing and market share;
- the ability of our U.S. partner to successfully distribute and sell Consensi;
- our ability to successfully obtain approvals for marketing of Consensi in other territories than the U.S.;
- 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 regulatory approval of our oncology therapeutic candidates or any other therapeutic candidates that we may acquire or develop in the future and addressing regulatory and other issues that may arise post-approval for such oncology therapeutic candidates or from commercializing Consensi;
- 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 and our sales, marketing and distribution channels;
- 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 approved products, or 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;
- patient acceptance of and demand for Consensi;
- sufficient coverage and reimbursement by third-party payers; and
- maintaining FDA marketing approval of Consensi.

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 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. A number of 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 its therapeutic candidates.

Our drug 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 drug 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 drug 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.

Although we commenced sales of Consensi in the U.S. market in May 2020, to date we have not achieved significant sales in the U.S. or marketed, distributed or sold any therapeutic candidate or drug product in any other territory. In addition to the agreement we entered into to distribute Consensi in the U.S., we have entered into only two other out-licensing agreements for marketing, manufacturing and distribution of Consensi in South Korea and China, which are dependent upon achieving regulatory clearance or approval for Consensi in each of those respective countries. 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. For example, even though the FDA has granted its approval to market Consensi for certain indications of use, the South Korean and/or the Chinese regulatory authorities may impose additional requirements or place other limitations on the indications for use in such countries before our licensee and distributors in such countries may commence manufacturing and selling Consensi. 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.

Pre-clinical 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 studies and clinical trials 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 the 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. The CMC, 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, the CMC, preclinical studies, and/or clinical trial process that could delay or prevent commercialization of our current or future therapeutic candidates.

In connection with the CMC, 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;
- 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;
- failure to manufacture our drug products, to maintain the drug products, or contamination to our drug products;
- 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;
- 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;
- 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 drug 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, or otherwise raise substantial additional capital, we will likely need to alter our development and any commercialization plans.

Our drug development programs, including our commercialization of Consensi and 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 to assist us in furthering development and potential commercialization of our therapeutic candidates, in some or all jurisdictions. While we have entered into an exclusive marketing and distribution agreement with respect to the commercialization of Consensi in the U.S. and market and out-licensing agreements for marketing, manufacturing and distribution of Consensi in South Korea and China, we may not be successful in collaborations with other third parties on acceptable terms, or at all. In addition, if we fail to negotiate and maintain suitable development 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 or Consensi 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, or failure to market and commercialize our Consensi drug product in the U.S. market, 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 Consensi drug product, 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. 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 Consensi drug product, 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;
- 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 drug candidates that have mostly not yet been administered to 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 are currently focused on combination products and drug candidates that have mostly not yet been administered to humans. Consensi has the combination of generic substances celecoxib and amlodipine besylate that had not previously been combined into one FDA-approved drug product or used at all in a clinical setting outside the scope of the clinical trials before we obtained FDA-approval to commercialize Consensi. We cannot be certain that the market will consider our Consensi drug product to be superior to the current gold standard of care or to treatment with the separate drug components rather than in combination.

The previous owners of the CM24 conducted the first human clinical trials for this therapeutic candidate, which were initiated in 2015, and discontinued in 2017. In the second half of 2020 we commenced a phase 1/2 study of NT219 as a single agent in patients with solid tumors, followed by a dose escalation phase of NT219 in combination with cetuximab for the treatment of recurrent and/or metastatic solid tumors and squamous cell carcinoma of the head and neck cancer or colorectal adenocarcinoma, and an expansion phase of NT219 at its recommended phase 2 level in combination with cetuximab in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck. However, we cannot be certain whether NT219 or CM24 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 a particular cancer treatment, or any other therapeutic candidate that we may develop or acquire in the future to be superior to the 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 drug candidates could have an adverse effect on our business, financial condition and results of operations.

In addition, as part of our strategy for growth, we may consider the acquisition of therapeutic candidates at various stages of development and in a variety of therapeutic areas, and we may also 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. 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 drug 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 we rely mainly on third parties, such as contract manufacturing organizations, contract research organizations, 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, contract research organizations 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 the CMC, 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, clinical development and commercialization of our therapeutic candidates would 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 completely 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 APIs to be compliant with the International Conference of Harmonization Q7 guidance and applicable laws and regulations, in the quantities we require on a timely basis.

We currently do not manufacture any API ourselves. Instead, we rely on third-party vendors for the manufacture and supply of our APIs that are used to formulate our Consensi drug product and our oncology therapeutic candidates. While there are many potential API 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 manufacturing of our drug product or in conducting clinical trials for NT219, CM24 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 in the market, we have not conducted extensive audits and investigations into the quality or availability of their APIs. In addition, we may acquire therapeutic candidates which already have long term commitments to a specific API supplier. As a result, we can provide no assurances that supply sources will not be interrupted from time to time. Changing API manufacturers or suppliers or finding and qualifying new API manufacturers or suppliers can be costly and take a significant amount of time. Many APIs 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, we may not be able to produce enough supplies of our Consensi drug product to meet the current or future demands of the public or 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 or any other therapeutic candidates we may develop or acquire in the future.

To date, our NT219 and CM24 therapeutic candidates has 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 successfully to 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 successfully to 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 anticipate continued reliance on third-party manufacturers to manufacture our Consensi drug product at commercial scale to meet the demand in the United States or any foreign jurisdiction in which we may commercialize our Consensi drug product in the future.

Prior to our U.S. launch of Consensi we engaged a third party supplier for the manufacturing of sufficient quantities of Consensi at commercial scale. We anticipate that we will continue to rely on our third-party manufacturer to manufacture our Consensi drug product at commercial scale under cGMP conditions. Our third-party supplier may not be able to successfully increase the manufacturing capacity for our Consensi drug product to meet the demand in the United States. Though we can attempt to ensure the availability of suppliers or manufacturers for Consensi, the number of suppliers with suitable manufacturing capacity and capability is often very limited, and therefore we may be dependent on one or a few such suppliers. Furthermore, any changes to the manufacturing process to increase the manufacturing capacity for Consensi, including changing or including additional manufacturers, or any other changes with respect to manufacturing may require additional validation studies, which the FDA must review and approve. If third-party manufacturers are unable to successfully increase the manufacturing capacity for Consensi or we are unable to establish alternative manufacturing capabilities, our efforts to meet the demand for our Consensi drug product in the United States 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 Consensi drug product and our oncology therapeutic candidates when we initiate their clinical trials. We and our manufacturers may not be able to comply with applicable laws, regulations and guidelines. We and our 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 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 FDA-approved Consensi drug product and 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, we could lose the FDA and/or other regulatory agencies' approval(s) we have obtained (or will obtain, if any), and our business would be seriously harmed.

Our FDA-approved Consensi drug product is subject to ongoing post-marketing surveillance programs and regulatory review. In addition, 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 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 or regulations may be enacted or changed that could hinder our ability to commercialize our Consensi drug product. 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 Consensi drug product and/or 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 and other civil or criminal sanctions, including fines and penalties.

Regulatory approval of our Consensi drug product is 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 Consensi (or other products or product candidates, as applicable) 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. We received FDA approval to commercialize Consensi only for the simultaneous treatment of two clinical conditions: pain caused by osteoarthritis and hypertension, or high blood pressure. Marketing or commercializing Consensi to treating a new symptom, or indication that is not pain caused by osteoarthritis and hypertension 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 rely on physicians to prescribe and administer Consensi as the product labeling directs and for the indications described on the labeling. To the extent any physicians prescribe Consensi to patients for off-label uses, or the use of Consensi departs from the approved uses, this may increase the risk of injury or other adverse events to the patients and product liability claims brought 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, the use of Consensi for indications other than those approved by the FDA or foreign authorities, if any, may not effectively treat the conditions associated with the off-label 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 Consensi 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 Consensi 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 Consensi 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 also requires that our and our 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.

Modifications to our Consensi drug product or to our oncology therapeutic candidates or any other therapeutic candidate(s) that we may acquire or develop in the future, if approved, will likely require new regulatory approvals before we may continue marketing such product or may require us, or our current or potential development and commercialization partners, as applicable, to recall or cease marketing our Consensi drug product or such therapeutic candidates until approvals are obtained.

Modifications to our Consensi drug product, our oncology therapeutic candidates or any other therapeutic candidate(s) that we may acquire or develop in the future, after they have been approved for marketing, if at all, may require new regulatory approvals, and may result in the recall or suspension of marketing of the product until clearances or approvals of the modified product are obtained. The FDA and other foreign regulatory authorities require manufacturers of approved drugs to make and document a determination of whether or not a modification requires a Prior Approval Supplement, a Changes Being Effected in 30 Days Supplement, or a report in the subsequent Annual Report depending on the impact of the change to the identity, strength, quality, purity, or potency of the approved drug product. A manufacturer may determine in conformity with applicable laws, regulations and guidelines that a modification may be implemented without approval of a Prior Approval Supplement by the FDA or a similar supplement submitted to other foreign regulatory authorities; however, the FDA or other foreign regulatory authorities may disagree with the manufacturer's decision. The FDA or other foreign regulatory authorities may also on their own initiative determine that an approval is required before commencing commercialization of the modified drug product. If the FDA or other foreign regulatory authorities require an approval of any drug product for which we or our current or potential development and commercialization partners previously received marketing approval, we or our current or potential development and commercialization partners may be required to recall such drug product and to stop marketing the drug product as modified, which could require us or our current or potential development and commercialization partners to redesign the therapeutic candidate and cause a material adverse effect on our business, financial condition and results of operations.

CM24 and NT219 may encounter substantial delays in their respective clinical trials or we may not be able to conduct their trials on the timelines we expect.

Clinical testing is expensive, time-consuming, and subject to uncertainty. We cannot guarantee that any CM24, NT219 and/or future drug candidates' clinical studies will be conducted as planned or completed on schedule, if at all. We intend to resume clinical testing of CM24 and continue clinical testing for 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 CM24's or NT219's future clinical studies 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;
- imposition of a temporary or permanent clinical hold by regulatory agencies;
- delays in recruiting suitable patients to participate in NT219's, CM24's or future drug candidates' clinical studies;
- 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 being greater than we anticipate;
- clinical studies of CM24, NT219 and/or future drug 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 drug candidates for use in clinical studies or the inability to do any of the foregoing, including any quality issues associated with contract manufacturers.

In addition, the Coronavirus (COVID-19) pandemic has affected the conduct of clinical trials of investigational therapeutic candidates by causing, among other things, slowdowns in site activities, difficulties or slowdown in patient enrollment, travel limitations, and other limitations for site personnel or trial subjects who became infected with COVID-19, all which has led to difficulties in performing studies. This may lead to difficulties in meeting protocol-specified procedures, including administering or using the therapeutic candidate or adhering to protocol-mandated visits and laboratory/diagnostic testing, unavoidable protocol deviations due to COVID-19 illness and/or COVID-19 control measures, which will likely vary depending on many factors, including the nature of disease under study, the trial design, and in what region(s) the study is being conducted.

We also may conduct clinical research in collaboration with other biotechnology and biologics entities in which we combine CM24 and/or NT219 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. These combination therapies will require additional testing and clinical trials will require additional FDA regulatory approval and will increase our future expenses.

Any inability to successfully complete clinical development could result in additional costs to us or impair our ability to generate revenue from our acquisition of CM24. In addition, if we make manufacturing or formulation changes to CM24, 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.

It may take longer and cost more to complete CM24 and/or NT219 clinical trials than initially projected, or we may not be able to complete them at all.

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 products as projected or may not conduct them successfully.

We may experience difficulties in patient enrollment in our future clinical trials for a variety of reasons, including as a result of the COVID-19 pandemic. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. In addition, 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 will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. 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.

We expect to rely on medical institutions, academic institutions, or clinical research organizations to conduct, supervise, or monitor some or all aspects of clinical trials involving our products. 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 COVID-19 on the ability of patients to visit the testing sites and the effect of the disease on potential patients who contracted the disease.

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 its therapeutic candidates.

We will depend on a joint collaboration partner to conduct clinical trials with CM24, and we may enter into future collaboration agreements with collaboration partners to develop and conduct clinical trials with, obtain regulatory approvals for, and market and sell the CM24 or other 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 collaboration partners, which we may not be able to engage in a timely manner, or 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 agreement with Bristol Myers Squibb Company (NYSE:BMY), for a planned phase 1/2 study of CM24 in combination with a PD-1 antibody nivolumab (Opdivo), and pursuant to an amendment to the agreement we signed on November 4, 2020, we expanded the phase 1/2 clinical trial to also evaluate CM24 and nivolumab, together with nab-paclitaxel (ABRAXANE), in patients with pancreatic cancer. We expect to initiate that study in 2021. We rely, and may in the future continue to rely, on our collaboration partners to develop, conduct clinical trials of, and commercialize our therapeutic candidates and approved products. 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 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. A collaboration partner may have the right to terminate its collaboration agreements. Any such termination of any agreement or any future agreement that we may enter into with collaboration partners could have a material adverse effect on our business, financial position and results of operations.

The manufacture of our drug 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 for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

NT219 is a chemical and CM24 is a biologic, and the process of manufacturing each is complex, highly regulated and subject to multiple risks. The manufacture of each of NT219 and CM24 involves complex processes, and ultimately infusing such product into a patient. As a result of the complexities, the cost to manufacture biologics such as CM 24 is generally higher than traditional small molecule chemical compounds, and the manufacturing process is less reliable and is more difficult to reproduce. Even minor deviations from normal manufacturing processes for each of NT219 and CM24 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 NT219’s and CM24’s clinical development and/or commercialization plans. We may ultimately be unable to reduce the cost of goods for each of NT219 and CM24 to levels that will allow for an attractive return on investment if and when those therapeutic candidates are commercialized.

Because CM24 and NT219 each 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 CM24 and NT219.

There is no assurance that the approaches offered by CM24 and NT219 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 CM24 and NT219 each represents new approaches 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 CM24 or NT219 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 CM24 and NT219, and the actual cost to manufacture these products could materially and adversely affect the commercial viability of these products. Our goal is to reduce the cost of manufacturing CM24 and NT219. However, unless we are able to 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 CM24 and NT219 based upon this approach or find suitable and economical sources for materials used in the production of these therapeutic candidates, the CM24 and NT219 therapeutic candidates will not become profitable.

The CM24 and NT219 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 CM24 and NT219 based therapy 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 license agreements, or disputes arise with respect to those agreements, it could have a negative impact on our business and our intellectual property rights.

We are a party to a license agreement with each of Yissum Research and Development Company of the Hebrew University of Jerusalem Ltd. ("Yissum"), the technology transfer company of the Hebrew University of Jerusalem, and Tel Hashomer – Medical Research Infrastructure and Services Ltd. ("THM") that 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 it 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 its licensors and collaborators;
- the scope and duration of our payment obligations;
- 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, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements.

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, our shareholders will 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. 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. 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.

We may be subject to additional risks because Consensi is a combination of two FDA-approved drugs.

Consensi is comprised of two FDA-approved drugs, celecoxib (the active ingredient in Pfizer's Celebrex) and amlodipine besylate (the active ingredient in Pfizer's Norvasc). Either of these two drugs could independently be found defective or, for a number of other reasons beyond our control, removed from the market and, thus, become unavailable for commercial use as a component of Consensi. Additionally, adverse action of any kind against one of the companies responsible for the drugs of which Consensi is comprised could affect our ability to obtain the applicable drug and/or public perception of us and/or Consensi based on our association with the company at-issue or the use of the applicable drug as a component of Consensi.

If we cannot meet our obligations under our in-license agreement with Yissum, or if other events occur that are not within our control, we could lose our rights to our NT219 therapeutic candidate, experience delays in developing or commercializing our NT219 therapeutic candidate or incur additional costs, which could have a material adverse effect on our business, financial condition and results of operations.

We license rights to our NT219 therapeutic candidate from Yissum pursuant to a license agreement. If we do not meet our obligations under this license agreement, or if other events occur that are not within our control, we could lose the rights to our NT219 therapeutic candidate, experience delays in developing or commercializing our NT219 therapeutic candidate or incur additional costs, any of which could have a material adverse effect on our business, financial condition and results of operations.

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

We own the rights to FDA-approved drug Consensi which we acquired as a therapeutic candidate in 2013, our NT219 therapeutic candidate which we acquired in 2017, and our CM24 therapeutic candidate which we acquired in 2020, each of which was acquired by us from a third party. 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.

The recent coronavirus outbreak may adversely affect our revenues, results of operations and financial condition.

In December 2019, a strain of coronavirus (COVID-19) surfaced in Wuhan, China, and in March 2020, the World Health Organization declared COVID-19 a pandemic and recommended containment and mitigation measures worldwide. COVID-19 has subsequently reached multiple countries, resulting in government-imposed quarantines, travel restrictions and other public health safety measures worldwide, including Israel. The various precautionary measures taken by many governmental authorities around the world in order to limit the spread of COVID-19 have had an adverse effect on the global markets and global economy, including on the availability and pricing of resources, materials, manufacturing and delivery efforts and other aspects of the global economy. The Israeli Ministry of Health has implemented various outbound travel restrictions, inbound quarantine requirements for passengers arriving from certain countries and/or events in other countries, including not allowing certain foreign nationals to disembark in Israel, as well as ordering curtailment of public gatherings, trade and other activities within Israel.

The impact of the COVID-19 pandemic on the conduct of clinical trials of our therapeutic candidates, and the challenges that have arisen, for example, from quarantines, travel limitations, and other considerations from site personnel or trial subjects becoming infected with COVID-19, have led to a slowdown of clinical trials (and slowed patient enrollment in the trials that we have conducted) and development activities. The impact of the pandemic may also lead to difficulties in meeting protocol-specified procedures, including administering or using the therapeutic candidate or adhering to protocol-mandated visits and laboratory/diagnostic testing, unavoidable protocol deviations due to COVID-19 illness and/or COVID-19 control measures, which will likely vary depending on many factors, including the nature of disease under study, the trial design, and in what region(s) the study is being conducted.

The COVID-19 pandemic may in the future disrupt production and cause delays in the supply and delivery of products used in our operations, affect our operations (including the conduct of clinical studies), the ability of regulatory bodies to grant approval, review our submissions or supervise our candidates and products, divert the attention and efforts of the medical community to coping with COVID-19 and disrupt the marketplace in which we operate, and may have a material adverse effects on our operations.

While the COVID-19 pandemic has not materially affected our operations to date, the extent to which the COVID-19 pandemic shall impact our operations will depend on future developments. In particular, the continued spread of COVID-19 globally could materially adversely impact our operations and workforce, including our manufacturing activities, clinical trials and product sales, including the commercialization of Consensi, as well as our ability to continue to raise capital.

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 all of the members 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. 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. In addition, if we elect to independently commercialize any therapeutic candidate, we will need to expand our marketing and sales capabilities. 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 and, in certain instances, our shareholders as well. 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 in order 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, 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.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change which may affect approval and commercialization of our drug candidate, Consensi.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. In recent years, the regulatory framework in China regarding the pharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes in the future. There is uncertainty as to the regulatory approach in China with respect to combination drug products. Any such uncertainty, changes or amendments may cause delays in or prevent the market authorization or the successful commercialization of our Consensi drug product in China and reduce the current benefits we believe are available to us from our commercialization agreement with Hebei Changshan Biochemical Pharmaceutical Co., Ltd. (Changshan Pharma). Chinese authorities have become increasingly vigilant in enforcing laws in the pharmaceutical industry and any failure by Changshan Pharma to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may prevent the receipt of market authorization for Consensi in China or otherwise result in the suspension of the commercialization of Consensi in China.

Changes in the political and economic policies of the Chinese government may materially and adversely affect the commercialization of Consensi in China.

The Chinese economy differs from the economies of most developed countries in many respects, including the extent of government involvement, level of development, growth rate, control of foreign exchange and allocation of resources. Although the Chinese government has implemented measures emphasizing the utilization of market forces for economic reform, the reduction of state ownership of productive assets, and the establishment of improved corporate governance in business enterprises, a substantial portion of productive assets in China is still owned by the government. In addition, the Chinese government continues to play a significant role in regulating industrial development by imposing industrial policies. The Chinese government also exercises significant control over China's economic growth by allocating resources, controlling payment of foreign currency-denominated obligations, setting monetary policy, regulating financial services and institutions and providing preferential treatment to particular industries or companies.

While the Chinese economy has experienced significant growth in the past three decades, growth has been uneven, both geographically and among various sectors of the economy. The Chinese government has implemented various measures to encourage economic growth and guide the allocation of resources. Some of these measures may benefit the overall Chinese economy but may also have a negative effect on us and our products. For example, our commercialization of Consensi in China could be materially and adversely affected by government control over capital investments, changes in tax regulations, or as of yet unknown impacts of the coronavirus outbreak.

Our subsidiary, TyrNovo, has received and may continue to receive Israeli governmental grants to assist in the funding of its research and development activities.

Our subsidiary, TyrNovo, has obligations to the Israel Innovation Authority, or IIA (formerly known as the Office of the Chief Scientist of the Ministry of Economy and Industry) with respect to grants it received from the IIA connection with NT219 and other TyrNovo's technology, in an aggregate amount of approximately NIS 5.5 million (or approximately $1.71 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 grants, or Recipient Company(ies), are obligated to pay the IIA royalties from the revenues generated from the sale of products and related services developed in whole or in part as a result of a research and development program funded by the IIA at rates which are determined under the IIA's rules and guidelines (generally of 3% to 5% on sales of products or services developed under the approved programs, depending on the type of the Recipient Company, 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).

TyrNovo's technologies, including NT219, were developed, at least in part, with funds from IIA grants, and accordingly TyrNovo is obligated to pay royalties on sales of any of its IIA funded products and related services. In addition, the Government of Israel may, from time to time, audit sales of products which it claims incorporate technology and know-how funded via IIA programs and this may lead to additional royalties being payable on additional products. As of December 31, 2020, the maximum royalty amount that would be payable by TyrNovo, excluding interest, is approximately NIS 5.5 million ($1.71 million), and as of such date TyrNovo had not paid any royalties to the IIA.

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.

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.

The research and development efforts underlying TyrNovo's technology including NT219 have been financed, in part, through the grants received from the IIA. TyrNovo, therefore, must comply with the requirements of the Innovation Law and the IIA's rules and guidelines.

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 may not receive the required approvals for any proposed transfer of manufacturing activities. This restriction may impair TyrNovo's ability to outsource manufacturing rights abroad.

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 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. It may also require TyrNovo to obtain the approval of the IIA for certain actions and transactions and pay additional royalties and other amounts to the IIA. 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.

Risks Related to Our Industry

Even though Consensi received regulatory approval in the United States and even if our oncology therapeutic candidates or any other therapeutic candidate that we develop in the future receive regulatory approval or do not require regulatory approval, they may not become or remain commercially viable products.

Even though Consensi is approved by the FDA for marketing in the United States, it may not be a commercially viable product that is accepted by physicians and patients in the United States. Even though we believe that the FDA approved Consensi for a commercially viable purpose in the simultaneous treatment of pain caused by osteoarthritis and hypertension, we cannot predict whether the FDA may limit the use of Consensi to treatments that are not commercially viable, which would severely affect our operations and revenue.

Likewise, even if 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 in the future, 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.

Physicians, various other health care providers, patients, payers or the medical community in general may be unwilling to accept, utilize or recommend Consensi, our oncology therapeutic candidates or any other therapeutic candidates that we may develop or acquire in the future. If we are unable, either on our own or through third parties, to manufacture, commercialize and market such products when planned, or develop or acquire commercially viable therapeutic candidates, we may not achieve any market acceptance or generate revenue.

The markets for our Consensi drug product and 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 Consensi and for which we are currently developing our other 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 Consensi drug product or our therapeutic candidates.

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 Consensi drug product or 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 Consensi, NT219, CM24 or other therapeutic candidates that we may develop 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.

For example, since 2010, the opioid epidemic in the United States has increasingly been recognized as a major cause of death. The CDC estimates that from 2010 to 2016 over 600,000 Americans died from opioid overdoses, and that in 2017, this number reached 70,237. As a result, individuals, corporations, and the FDA have increasingly sought to decrease the over utilization of opioids. One method for decreasing the use of opioids is to increase the use of other analgesics. We believe that Consensi could potentially replace opioids for many types of chronic pain. However, it is possible that new drugs and new treatments that have been developed or that are in the process of being developed by others in order to reduce the use of opioids may render Consensi noncompetitive in this market.

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 Consensi drug product or our therapeutic candidates to receive widespread acceptance.

If third-party payers do not adequately reimburse customers for our Consensi drug product, or our oncology therapeutic candidates, if approved, or any of other therapeutic candidates that may be approved for marketing in the future, 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 Consensi drug product that is approved for commercialization, and of our oncology therapeutic candidates, if approved, or any of other therapeutic candidates that may be approved for marketing in the future, if at all, from governmental and/or other third-party payers, both in the U.S. and in foreign markets. Our Consensi drug product has not yet received reimbursement from all government or other third party payers. 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.

It has been reported that generic drug prices have generally fallen in the past few years. When this has occurred, profits of certain generic drug companies, such as Teva Pharmaceuticals (NYSE:TEVA; TASE:TEVA), have also generally fallen. With the decrease in profits, the stock prices of publicly traded generic pharmaceutical companies have in the past often fallen in tandem. It is unclear to us what effect this might have on the marketing of Consensi which, while patented, is comprised of two separate generic drug components.

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 Consensi drug product in the U.S. or our oncology therapeutic candidates, if approved. We believe that legislation that reduces reimbursement for our Consensi drug product or our oncology therapeutic candidates, if approved, could adversely impact how much or under what circumstances healthcare providers will prescribe or administer our Consensi drug product, or 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 Consensi drug product, or 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.

A number of legislative and regulatory changes in the healthcare system in the U.S. have been proposed and adopted in recent years, and efforts of the legislature and third-party payers to contain or reduce the cost of healthcare and broaden the availability of healthcare continue. These developments could, directly or indirectly, affect our ability to sell our Consensi drug product or our oncology therapeutic candidates, if approved, in the U.S. On March 23, 2010, the Patient Protection and Affordable Care Act (P.L. 111-148) was signed into law, followed by the Health Care and Education Reconciliation Act (P.L. 111-152) on March 30, 2010 (referred to, collectively, as the “Healthcare Reform Law”). The Healthcare Reform Law was enacted with the intent to broaden access to health insurance, reduce or constrain the growth of health spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare industry, impose new taxes and fees, and impose additional policy reforms, among others. In addition, the Healthcare Reform Law included a number of new rules regarding health insurance, the provision of healthcare, and conditions to reimbursement for healthcare services provided to Medicare and Medicaid patients and other healthcare policy reforms, largely designed to encourage providers to find cost savings in their clinical operations.

The Healthcare Reform Law sparked one of the most comprehensive and significant reforms in the history of the U.S. healthcare industry, has significantly changed the way healthcare is financed and has impacted the scope of healthcare insurance and incentives, among others. Pharmaceuticals represent a significant portion of the cost of providing healthcare. The environment created by the Healthcare Reform Law 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 in relation to pharmaceuticals. This attention may result in our Consensi drug product or our oncology therapeutic candidates, if approved, being chosen less frequently or the pricing being substantially lowered.

Certain facets of the Healthcare Reform Law and subsequent legislation, such as the extension of medical benefits to those who previously lacked coverage may, in the long term, result in substantial costs to the U.S. government, which may force significant additional changes to the U.S. healthcare system. Much of the funding for expanded healthcare coverage may be sought through cost savings. While some of these savings may come from realizing greater efficiencies in delivering care, improving the effectiveness of preventive care and enhancing the overall quality of care, much of the cost savings may come from reducing the cost of care and increased enforcement activities. Cost of care could be reduced further by decreasing the level of reimbursement for medical services or products (including our Consensi drug product or those oncology therapeutic candidates currently being developed by us or our development or commercialization partners, if approved), or by restricting coverage (and, thereby, utilization) of medical services or products. Continued restructuring of medical care coverage in the U.S. could further impact the reimbursement for the types of prescribed drugs and pharmaceuticals that we and our development or commercialization partners are developing. If reimbursement or utilization for our Consensi drug product or our oncology therapeutic candidates (if approved) is substantially reduced or otherwise adversely affected in the future, or rebate or similar obligations or fees associates with them are imposed or substantially increased, it could have a material adverse effect on our business, financial condition and results of operations.

Further, the U.S. healthcare environment has seen significant changes in recent years and is still in flux. Judicial challenges as well as legislative initiatives to modify, limit, or repeal the Healthcare Reform Law have been initiated and continue to evolve. For example, former President Trump issued an executive order in which he stated that it is his administration’s policy to seek the prompt repeal of the Healthcare Reform Law and in which he directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the Healthcare Reform Law to the maximum extent permitted by law. Congress has enacted legislation that repeals certain portions of the Healthcare Reform Law, including but not limited to the Tax Cuts and Jobs Act, passed in December 2017, which included a provision that eliminates the penalty under the Healthcare Reform Law’s individual mandate, effective January 1, 2019, as well as the Bipartisan Budget Act of 2018, passed in February 2018, which, among other things, increases pharmaceutical manufacturers’ discount in the Coverage Gap Discount Program from 50% to 70% of the negotiated price of applicable drugs.

Additionally, in December 2018, a district court in Texas held that the individual mandate is unconstitutional and that the rest of the Healthcare Reform Law is, therefore, invalid. On appeal, the Fifth Circuit Court of Appeals affirmed the holding on the individual mandate but remanded the case back to the lower court to reassess whether and how such holding affects the validity of the rest of the Healthcare Reform Law. Substantial uncertainty remains as to the future of the Healthcare Reform Law as the case was appealed to the U.S. Supreme Court and currently awaiting a ruling. It is unknown whether, and to what extent, if any, the Healthcare Reform Law will remain in-effect in the future, and it is unclear how judicial decisions, subsequent appeals, legislative or executive measures, or other efforts to repeal and replace or, possibly, to restore the Healthcare Reform Law will impact the U.S. healthcare industry or our business.

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 our Consensi drug product and 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 our approved products. The laws that may affect our ability to operate 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 and teaching hospitals and ownership or investment interests held by physicians or 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 current 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 Consensi drug product, or 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 Consensi drug product, or 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 Consensi drug product, or 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 Consensi drug product, or 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 completely 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.

Risks Related to Legal Proceedings and Intellectual Property

Legal proceedings or 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 claim or other legal challenges could have a material adverse effect on our business, results of operations and 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 not possible 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 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.

On December 21, 2020, Bar Ilan University and BIRAD Research & Development Company Ltd. (the “University” and “BIRAD”, respectively) filed a statement of claim to the court against TyrNovo, the Company, its officers and others. In the claim, the petitioners allege that the University is the rightful owner of a patent owned by TyrNovo. The main remedy sought by the petitioners is a declaratory relief under which the University is declared the owner of such patent. We plan to file our response in April 2021, when it is due. At this preliminary stage we are unable, with any degree of certainty, to make any evaluations or any assessments with respect to the probability of success or the scope of potential exposure, if any.

On August 4, 2020, Lupin Ltd. and Lupin Pharmaceuticals USA, Inc. (together, “Lupin”) notified Purple and Coeptis Pharmaceuticals, Inc. (“Coeptis”), our distribution partner for Consensi, that it had filed an Abbreviated New Drug Application (“ANDA”) with the FDA to market a generic version of Consensi. Lupin also sent both parties a Paragraph IV Notice Letter alleging that certain of our patents are invalid and/or not infringed by Lupin’s proposed generic product. In September 2020, we filed a complaint in the United States District Court for the District of New Jersey against Lupin and claimed that Lupin’s proposed generic product infringes certain of our patents and sought declaratory and injunctive relief. On January 12, 2021, the court issued an order providing a schedule for the briefs and other items to be submitted, and the discovery to be conducted, by the parties, which will take place over the course of 2021.

From time to time, we may also be involved in various lawsuits and legal proceedings other than intellectual property infringement actions, concerning such laws as corporate and securities laws, business laws, product liability laws, and environmental laws. On December 3, 2015, we announced that we received a lawsuit and motion to approve the lawsuit as a class action lawsuit pursuant to the Class Action Lawsuits Law 5766-2006 which was filed against us and our directors at the Tel Aviv District Court (Economic Division). The motion asserts claims for damages to the holders of our securities listed on the TASE, arising due to the initial public offering of our securities in the U.S. during November 2015. A separate, similar claim in the amount of NIS 1.1 million was filed against us in May 2018 by an individual shareholder seeking to separate from the purported class in the original motion. Additionally, on February 16, 2017, we announced that four lawsuits and motions to approve the lawsuits as a class action lawsuit (one of which was later withdrawn, and the remainder of which were later consolidated into one motion) were filed against us and certain of our office holders in the Tel Aviv District Court (Economic Division), and served on us, with each such motion relating to the former investigation by the Israel Securities Authority (“ISA”) into certain of our public disclosures (all of the motions above collectively, the “Israel Motions”).

In addition, in February 2017 class actions lawsuits largely relating to the same matters were filed in the State of California and in the U.S. district court for the Southern District of New York against us, our CEO and former CFO, and in the California lawsuits, against the underwriters of our November 2015 initial public offering in the U.S.A. (collectively, the "US Motions"). We finalized a settlement agreement with respect to the US Motions, which was approved by the court on March 22, 2019. Under the terms of the settlement, the classes in all of the actions received aggregate consideration of $2.0 million (the "US Settlement"), all of which, as well as ancillary expenses, were funded by our insurance carriers. Pursuant to the US Settlement, we and our directors and officers as well as the other defendants named in the actions were released from the claims that were asserted or could have been asserted in the actions by class members participating in the settlement. The US Settlement contains no admission of wrongdoing and reiterates that we have always maintained and continue to believe that we did not engage in any wrongdoing or otherwise commit any violation of federal or state securities laws or other laws.

In Israel, we were previously subject to a formal investigation by the ISA (the "ISA Investigation") into our public disclosures around certain aspects of the studies related to our therapeutic candidate, Consensi. On August 13, 2019, the Administrative Enforcement Committee (the "Committee") of the ISA approved an administrative enforcement agreement, titled Enforcement Arrangement ("Enforcement Arrangement"), entered into by and amongst the ISA, Purple Biotech, Isaac Israel, our chief executive officer, Dr. Paul Waymack, our former chairman and Simcha Rock, our former chief financial officer and currently a director, pursuant to which the Company and each of Messrs. Israel, Waymack and Rock settled the ISA's claims that under Israeli Securities Laws the Company made negligent disclosures in a number of its historical reports filed with the ISA in 2014 and 2015, and the ISA decided to discontinue its criminal investigation and to cease all proceedings us and our principals. As part of the Enforcement Arrangement, the Company agreed to pay a fine of NIS 1,500,000 (approximately $430,000), payable in 24 consecutive monthly payments, of which $322,500 has been paid to date, and the different principals agreed to each pay a fine. Messrs. Israel and Rock each also agreed to be subject to a conditional prohibition to serve as a senior officer in a supervised body under the Israeli Securities Law for a period of 12 months in the event that he violates certain sections under the Israeli securities laws within two years.

While we do not expect the Enforcement Arrangement to have a material impact on the Company's statement of operations, we do not yet know to what extent it may have an impact on the proceedings being conducted under the Israel Motions which are still continuing at the Tel Aviv District Court. In addition, the ongoing proceedings described above could result in significant legal defense costs and high punitive damage payments. Although we maintain directors' and officers' liability insurance (with an extension to cover the Company as well) and which is expected to cover much of our expected costs (legal and otherwise) in connection with the ongoing lawsuits and outstanding payments described above, after payment by us of the policy deductibles, the insurance companies may reject our claims for coverage under the policy or the coverage may not be adequate to cover future claims. Furthermore, we were required to indemnify our underwriters for their legal defense costs or any other damages in the California lawsuits, and such indemnification was not covered under the policy. We paid our underwriters to indemnify them for their legal costs in connection with the California lawsuits an aggregate amount of approximately $186,900.

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.

It is difficult to foresee the results of legal actions and proceedings currently involving us or those which may arise in the future, and an adverse result in these matters could have a material adverse effect on our business, results of operations and financial condition. In addition, any legal or administrative proceedings which we are subject to could require the significant involvement of our senior management and may divert management attention from our business and operations.

We may be unable to adequately protect or enforce our rights to intellectual property, causing us to lose valuable rights. Loss of patent rights may lead us to lose market share and potential profits.

Our success depends, in part, on our ability, and the ability of our current or 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. 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 are seeking or intend to seek regulatory approval to market Consensi or our therapeutic candidates in a number of foreign countries, including China and South Korea. Consensi and our therapeutic candidates are not protected by patents in certain countries, including China where we are currently seeking patent protection and South Korea, 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 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 not protected by patents in China 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 the 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

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. and may not be enforced by an Israeli court. In addition, it may also 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. Israeli courts may refuse to hear a claim based on a violation of U.S. securities laws against us or our non-U.S. officers and directors because Israel may not be 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. As a result of the difficulty associated with enforcing a judgment obtained in the United States against us or our non-U.S. officers and directors in Israel, it may be impossible to collect any damages awarded by either a U.S. or foreign court.

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, subject to applicable law. The amount of the advance indemnity will not exceed 25% of our then consolidated shareholders' equity, per our most recent consolidated annual 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 or other claims which may be filed against our directors and officers, as well as the ISA Investigation, 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 "*Legal proceedings or 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 developing or commercializing our therapeutic candidates. An adverse result in these infringements and other legal challenges could have a material adverse effect on our business, results of operations and financial conditions*" under the risk factor section titled "Risks Related to Legal Proceedings and 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.

We conduct our operations in Israel and therefore our results may be adversely affected by political, economic and military instability in Israel and its region as well as COVID-19 protocols in Israel.

We are incorporated under the laws of the State of Israel, our principal offices are located in central Israel and most of our officers, employees, consultants and directors are residents of Israel. Accordingly, political, economic and military conditions in Israel and the surrounding region may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors. These conflicts have often involved missile strikes against civilian targets in various parts of Israel, and negatively affected business conditions in Israel. The tension between Israel and Iran or extremist groups in the region, such as Hamas in Gaza and Hezbollah in Lebanon, may escalate in the future and turn violent, which could affect the Israeli economy generally and us in particular.

Any hostilities involving Israel, or pandemics impacting Israel and its economy (such as the COVID-19 pandemic), related travel restrictions or quarantine, 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. Parties with whom we may do business have sometimes declined to travel to Israel during periods of heightened unrest or tension and have not been able to travel to Israel during the COVID-19 pandemic, forcing us to make alternative arrangements when necessary. The conflict situation in Israel, or COVID-19 (or other pandemic) related travel restrictions 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 or the COVID-19 (or other pandemic) related travel restrictions, 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.

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. Any losses or damages incurred by us could have a material adverse effect on our business. Any armed conflicts, terrorist activities or political instability in the region would likely negatively affect business conditions and could harm our results of operations.

Further, in the past, the State of Israel and Israeli companies have been subjected to an economic boycott. Several countries still restrict business and trade activity with the State of Israel and with Israeli companies, and additional countries may impose restrictions on doing business with Israel and Israeli companies if hostilities in the region continue or intensify. Such restrictions may seriously limit our ability to sell our products to customers in those countries.

If the current coronavirus outbreak continues and results in a prolonged period of travel, commercial and other similar restrictions to or from Israel could materially disrupt our business and operations, slow down the overall economy, and make it hard to adequately staff our operations.

Any of the factors set forth above may have an adverse impact on our operating results, financial condition or the expansion of our business.

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 or changes in our management. These provisions include matters in connection with the election and removal of directors, such as our staggered board of directors, the right of our board of directors to appoint additional directors to fill vacancies on the board of directors, the size of our board of directors, the terms of office of our directors and the special majority required to amend such provision in our amended and restated articles of association.

In addition, 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 of directors, which can establish conversion, redemption, optional and other special rights, qualifications, limitations or restrictions, if any, of the non-voting senior preferred 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 corporations, 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.

These and other similar provisions could delay, prevent or impede an acquisition of us or our merger with another company, or an acquisition of a significant portion of our shares, even if such an acquisition or merger would be beneficial to us or to our shareholders.

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 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. 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, the federal district courts of the United States for the District of New York shall 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 are 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, if our ordinary shares or ADSs are covered by analysts;
- changes in government regulations or patent decisions;
- developments by our current or potential development and commercialization partners; and
- general market conditions and other factors, including factors unrelated to our operating performance.

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 historically have been very volatile. The market for these listed securities has, from time to time, experienced significant price and volume fluctuations for reasons unrelated to the operating performance of any one company. 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 "*Legal proceedings or 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 claim or other legal challenges could have a material adverse effect on our business, results of operations and financial condition*."

Future sales of our ordinary shares or ADSs or other warrants or convertible securities could reduce the market price of our ordinary shares and ADSs.

As of March 7, 2021, we had an aggregate of 175,105,742 issued and outstanding ordinary shares (including 1 dormant ordinary share held in treasury), no non-voting senior preferred shares, 4,595,005 non-listed warrants to purchase 4,595,005 ADSs (representing 45,950,050 ordinary shares) issued to investors, the underwriters and placement agents as part of a number of public and registered direct offerings by us, warrants to purchase up to an additional 403,779 ADSs (representing 4,037,805 ordinary shares) issued by us in January 2020 to former shareholders of FameWave in connection with our acquisition of FameWave, and non-tradable options and restricted stock units to purchase 10,384,380 ordinary shares pursuant to our equity based incentive compensation plans and arrangements.

Any future sales by us or our shareholders of a substantial number of our ordinary shares or ADSs or other warrants or securities convertible into 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 options or the conversion of convertible securities, may cause the market price of our ordinary shares or ADSs or other listed securities to decline.

NASDAQ has a listing requirement of a minimum closing bid price of $1.00 per share. If our ADSs cannot maintain the required minimum closing bid price and we fail to correct the listing requirement deficiency within the provided cure period, our ADSs may be involuntarily delisted from NASDAQ.

Our ADSs are listed on NASDAQ, and the quantitative listing standards of NASDAQ require, among other things, that listed companies maintain a minimum closing bid price of $1.00 per ADS. On July 8, 2019, we received a letter from the Listing Qualifications Department of NASDAQ indicating that, based upon the closing bid price of our ADSs for the last 30 consecutive business days, 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). We were not able to regain compliance with this requirement within the 180-day period ending on January 6, 2020, but we were granted an extension until September 18, 2020, to regain compliance with this requirement. On August 21, 2020, we changed the ratio of our ADSs to ordinary shares from one (1) ADS representing one (1) ordinary share to a new ratio of one (1) ADS representing ten (10) ordinary shares, the primary purpose of which was to enable us to regain compliance with the $1.00 minimum bid price requirement. On September 4, 2020, we received a notification letter from Listing Qualifications Department of NASDAQ stating that it had determined that for ten consecutive business days (from August 21, 2020 through September 3, 2020), the closing bid price of our ADS had been at $1.00 per ADS or greater, and accordingly we had regained compliance with the minimum bid price for continued listing on NASDAQ.

Although we have regained compliance with the minimum bid price requirement, if we are unable to satisfy the minimum bid price requirement in the future and should a delisting occur, an investor would likely find it significantly more difficult to dispose of, or to obtain accurate quotations as to the value of our ADSs, and our ability to raise future capital through the sale of our ADSs could be severely limited. Delisting would also impact some of our disclosure obligations under Israeli law. Following a delisting, we would remain a publicly traded company on TASE and revert to being subject to full Israeli securities laws and disclosure requirements. Accordingly, we would need to comply with U.S. and Israeli disclosure requirements, which would likely lead to additional 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 shares of 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 our ADSs, which could severely limit the market liquidity of such 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 The NASDAQ Capital Market 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.

We ceased to qualify as an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or JOBS Act, as of December 31, 2020, which was the last day of our fiscal year following the fifth anniversary of the closing of our initial public offering on NASDAQ on November 25, 2015. As a result, we can no longer take advantage of certain temporary exemptions from various reporting requirements, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes Oxley Act (and the rules and regulations of the SEC thereunder). We expect to incur additional expenses and devote increased management effort toward ensuring compliance with such additional reporting requirements.

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, since we no longer qualify as an "emerging growth company" under the JOBS Act, our independent registered public accounting firm is also required to attest to the effectiveness of our internal control over financial reporting under Section 404.

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 of directors, 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 may be classified as a Passive Foreign Investment Company, or PFIC, for U.S. federal income tax purposes in 2021 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 2020 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. 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, 2021. In the future, we would lose our foreign private issuer status if (1) more than 50% of our outstanding voting securities are 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.

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

Our 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 our 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.

The effect of this discretionary proxy is that a holder of our 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 of directors 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 of directors 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 share and ADSs.

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 our ADSs may not receive any value for them, if it is illegal or impractical to make them available to investors in our ADSs.

The depositary for the ADSs has agreed to pay investors in our 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 our 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 our 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 our 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 our 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 our 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 our 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 our 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 our 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.

Our ADSs have a limited trading history in the U.S., and present level of market activity may not be sustained, which may limit the ability of our investors to sell our ADSs in the U.S.

Although our ADSs have been traded on NASDAQ since November 20, 2015, the present level of market activity for our ADSs may not be sustained. If an active market for our ADSs is not sustained, it may be difficult for an investor to sell its ADSs.

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 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 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 ADSs, the price of our ADSs could decline.

The trading market for our ADSs will rely in part on the research and reports that equity research analysts publish about us and our business. The price of our ADSs could decline if such research or reports are not published or if one or more securities analysts downgrade our 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 to expand our clinical development program, expand our clinical development pipeline for additional drug products, including by way of possible acquisitions, 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.

General Risk Factors

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. 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.