PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A.[Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

Our business and our industry are subject to significant risks. You should carefully consider the risks and uncertainties described below, together with all of the other information in this Annual Report, including our audited consolidated financial statements and related notes. This Annual Report also includes forward-looking statements that involve risks and uncertainties. See "Special Note Regarding Forward-Looking Statements." If any of the following risks are realized, our business, financial condition, operating results and prospects could be materially and adversely affected.

Summary of Key Risks

- Risks Related to Our Business
  - Our operating history, which has focused primarily on research and development and advancing the clinical trial program for NBTXR3, makes it difficult to assess our future prospects.
  - We have not generated significant revenues and have incurred significant operating losses since our inception. While the amount of our future net losses will depend, in part, on the amount of our future operating expenses and our ability to obtain funding, we anticipate that we will continue to incur significant losses for the foreseeable future.
  - Because each of our ongoing and contemplated clinical trials involves NBTXR3, we are heavily dependent on the successful development and commercialization of this lead product candidate.
  - We face significant competition in our discovery, development and commercialization activities from competitors who may have significantly greater resources than we do.
  - The extent to which the COVID-19 pandemic and resulting deterioration of worldwide economic conditions adversely impacts our business, financial condition, and operating results will depend on future developments, which are difficult to predict.
  - We will require additional funding, which may not be available on acceptable terms or at all, and certain financing instruments—such as the finance contract for the EIB loan (as defined herein)—may impose certain restrictions on the operation of our business.

- Risks Related to the Development of Our Product Candidates
  - Our product candidates must undergo clinical trials that are time-consuming and expensive, the outcomes of which are unpredictable and for which there is a high risk of failure, and which are susceptible under a variety of circumstances to additional costs, delays, suspensions and terminations.
  - We rely on third parties to assist in our discovery, development, commercialization and manufacturing of our product candidates and issues relating to such third parties, or their activities, could result in additional costs and delays and hinder our research, development and commercialization prospects.
  - In connection with collaboration agreements with third parties for the development and commercialization of our product candidates, we may be unable to identify suitable collaboration partners, and once a collaboration partner is secured, we have limited control over the attention that our commercialization partner devotes to our product candidates.

- Risks Related to Obtaining Regulatory Approval or Certification for Our Product Candidates
  - Our business is governed by a rigorous, complex and evolving regulatory framework, including stringent clinical trial regulations, pre-marketing regulatory requirements, pricing, reimbursement and cost-containment regulations, and rigorous ongoing regulation of approved products. This regulatory framework results in significant compliance costs, makes the development and approval of our product candidates time intensive and unpredictable, and may reduce the ultimate economic value and prospects for our product candidates.
  - A Fast Track or Breakthrough Therapy designation by the FDA may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive regulatory approval.

- Risks Related to the Production and Manufacturing of Our Product Candidates
  - Because we depend on third parties for the supply of various materials that are necessary to produce our product candidates for clinical trials, the loss of key suppliers, the unavailability of raw materials, or disruptions in manufacturing processes could increase production costs or result in delays in our product development.
  - Our and our subcontractors' manufacturing facilities are subject to significant government regulations and approvals and any compliance failures could lead to significant delays in the availability of products for commercial sale or clinical trials, may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of marketing applications or the completion of pre-marketing certification procedures, as applicable, for our products.

- Risks Related to the Commercialization of Our Product Candidates
  - Even if we successfully complete clinical trials for certain of our product candidates, those candidates may not be commercialized or achieve commercial success for a variety of reasons, including a lack of acceptance by the medical community, the imposition of post-marketing regulatory restrictions, the costs and burdens associated with post-marketing regulatory requirements, or unanticipated problems with our products following regulatory approval.
  - If we are unable to establish sales, marketing and distribution capabilities for our product candidates, we may not be successful in commercializing those product candidates if and when they are approved or duly CE marked.

- Risks Related to Human Capital Management
  - We may encounter difficulties in managing our development and expansion, including challenges associated with our ability to attract and retain executive management and supervisory board members as a U.S. public company.
  - Our business could be harmed if we lose key management personnel on whom we depend or if we cannot attract and retain other qualified personnel.
  - Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

- Risks Related to Operational Compliance and Risk Management
  - We use hazardous chemicals in our business, and any claims relating to improper handling, storage or disposal of these materials could be time-consuming and costly.
  - The risk of product liability claims is inherent in the development and commercialization of therapeutic products, and product liability or other lawsuits could divert management and financial resources, result in substantial liabilities and reduce the commercial potential of our product candidates.
  - We are subject to extensive healthcare laws and regulations impacting, among other things, our research and proposed sales, marketing and education programs of product candidates that successfully complete applicable pre-marketing regulatory requirements, and which may require substantial compliance efforts. Any regulatory compliance failures could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

- Risks Related to Intellectual Property
  - Because our commercial success depends, in part, on obtaining and maintaining proprietary rights to our and our licensors' intellectual property, our ability to compete may decline if we fail to obtain protection for our products, product candidates, processes and technologies or do not adequately protect our intellectual property.
  - Our competitive position may be adversely impacted as a result of a variety of factors, including potentially adverse determinations of complex legal and factual questions involved in patents and patent applications or insufficiently long patent lifespans in one or more jurisdictions where we obtain intellectual property protection.

- Because it is cost prohibitive to seek intellectual property protection on a global basis, our intellectual property protection in certain jurisdictions many not be as robust as in the United States, which may adversely impact our competitive position.
- Third parties may assert ownership or commercial rights to inventions we develop or otherwise regard as our own, or assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.
- A dispute concerning the infringement or misappropriation of our intellectual property rights or the intellectual property rights of others could be time-consuming and costly, and an unfavorable outcome could harm our business.

- Risks Related to the Ownership of Our Ordinary Shares and ADSs
  - We do not currently intend to pay dividends on our securities, and under French law may be limited in our ability to do so in the future.
  - Holders of ADSs will not be directly holding our ordinary shares and may be subject to limitations on the transfer of their ADSs and certain voting and withdrawal rights of the underlying ordinary shares as well as limitations on their ability to exercise preferential subscription rights or receive share dividends.
  - We are an emerging growth company and we cannot be certain if the reduced disclosure requirements applicable to us will make our ADSs less attractive to investors.
  - ADSs holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiffs in any such action.

- Risks Related to Our Status as a Non-U.S. Company
  - The rights of shareholders in companies subject to French corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.
  - As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and the Nasdaq's corporate governance standards. We expect to follow certain home country practices in relation to certain corporate governance matters, which may afford less protection than would be provided if we fully complied with the Nasdaq requirements.
  - Our By-laws and French corporate law contain provisions that may delay or discourage a takeover attempt.
  - If we are determined to be a PFIC for any taxable year, there may be adverse U.S. federal income tax consequences to U.S. holders.
  - Our international operations may be exposed to foreign exchange risks, U.S. federal income tax risks, and additional risks, and our exposure to these risks will increase as our business continues to expand.

Risks Related to Our Business

Our operating history makes it difficult to assess our future prospects.

Our operating history has been focused primarily on research and development and the advancement of the clinical trial program for our lead product candidate, NBTXR3. A key element of our strategy is to use and expand our proprietary technology to continue to develop our innovative product candidates designed to enhance the efficacy of radiotherapy and to progress these candidates through clinical development for the treatment of a wide variety of cancers, including STS, head and neck cancers, liver cancers, prostate cancer and rectal cancer. The nanotechnology underlying our product candidates, specifically the use of nano-sized radiation enhancers as a cancer treatment method, is novel.

Although in April 2019, we successfully completed the applicable conformity assessment procedure for affixing the CE marking to our NBTXR3 device for the treatment of locally advanced STS, enabling commercialization of the product in the European Union (the "EU") for such indication, we have not yet commercialized the product nor generated any revenues from the sale of any approved products and we may ultimately not be able to generate substantial revenue from the commercialization of approved products.

We have encountered, and will continue to encounter, risks and difficulties frequently encountered by growing companies in new and rapidly evolving fields, particularly as we seek to utilize nanotechnology to provide solutions to unmet therapeutic needs in oncology. Consequently, the ability to predict our future operating results or business prospects is more limited than if we had a portfolio of approved products on the market.

We may not be able to fully implement or execute on our commercial strategy or realize, in whole or in part or within our expected time frames, the anticipated benefits of our growth strategies. You should consider our business and prospects in light of the risks and difficulties we face as a growing company focused primarily on the development and advancement of clinical trials.

We have incurred significant losses and anticipate that we will continue to incur significant losses for the foreseeable future.

We have not generated significant revenues and have incurred significant operating losses since our inception. To date, our limited revenues and other income have been derived primarily from payments under our license and collaboration agreement with PharmaEngine, which terminated in March 2021 (see item 4B. Business overview - our collaboration agreements" for additional details), and research tax credits. We have not generated revenues to date from product sales or royalties, and we do not expect to generate significant revenues from product sales or royalties unless and until our product candidates are successfully commercialized following regulatory approval. We incurred net losses of €47.0 million for the year ended December 31, 2021. The amount of our future net losses will depend, in part, on the amount of our future operating expenses and the pace at which they are incurred and our ability to obtain funding through our commercialization activities, through equity or debt financings or through research grants or collaborative partnerships. As of December 31, 2021, our losses are primarily attributable to expenditures committed to developing our nanotechnology and our clinical and preclinical programs. We expect to continue to incur significant expenses and losses for the foreseeable future. We anticipate that such expenses and capital requirements will increase substantially as we:

- continue our preclinical and clinical programs currently in progress;
- expand the scope of our current clinical trials and commence new clinical trials to research new oncological applications for our nanotechnology;
- expand our manufacturing capabilities for the production of our product candidates and maintain compliance with applicable manufacturing regulatory requirements;
- seek regulatory and marketing approvals, or initiate the necessary conformity assessment procedures, as applicable, for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may successfully complete applicable pre-marketing regulatory requirements;
- advance our research and development efforts, which may include the acquisition of new technologies, products or licenses;
- maintain, protect and expand our intellectual property portfolio; and
- attract new and retain existing skilled personnel.

The net losses we incur may fluctuate significantly from year-to-year such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular period or periods, our operating results could be below the expectations of securities analysts or investors, which could cause the price of our ordinary shares and ADSs to decline.

We are heavily dependent on the successful development and commercialization of NBTXR3.

Our business and future success depends heavily on our ability to develop and commercialize our lead product candidate, NBTXR3, for indications for which there is an attractive market opportunity, and to satisfy the necessary regulatory requirements for its marketing and sale. Our development programs of NBTXR3 for the treatment of different cancer indications are at varying stages. Because each of our ongoing and contemplated trials involves NBTXR3, if one of these preclinical or clinical trials reveals safety and/or therapeutic efficacy issues, the validity of our nanotechnology platform itself could be questioned, which could potentially require additional time and investment in research and development to attempt to remedy the issues identified. The development of each application of NBTXR3 could subsequently be impacted, potentially having a significant negative impact on our business prospects, financial situation and anticipated growth.

Although we successfully completed the applicable conformity assessment procedure for affixing the CE marking to our NBTXR3 device for the treatment of locally advanced STS, enabling the commercialization of the product in the EU for such indication, NBTXR3 remains in clinical development for other indications, and we cannot be certain that NBTXR3 will receive regulatory approval or successfully complete the necessary conformity assessment procedures, as applicable, or be successfully commercialized, for any additional cancer indications, even if we successfully complete applicable pre-marketing regulatory requirements. Any failure or delay in the development or commercialization of NBTXR3 could have a material adverse effect on our business, financial condition and prospects.

We face competition and our competitors may have significantly greater financial, technical and other resources than we do, which may result in others discovering, developing, receiving approval for, or commercializing products before or more successfully than us.

The development of treatments for cancer is subject to rapid technological change. Many companies, academic research institutions, governmental agencies and public and private research institutions are pursuing the development of medicinal products, devices and other therapies that target the same conditions that we are targeting, including in some cases in the same patient populations that we are targeting. Certain companies are developing treatments to increase sensitivities of tumors to radiation and other sources of energy. Like us, these companies are pursuing various technologies that involve substances that work to destroy tumor cells from the inside without causing additional damage to surrounding healthy tissues. Any product candidates that we develop and commercialize may compete with existing therapies, as well as new therapies that may become available in the future, including therapies with a mode of action similar to that of NBTXR3.

Many of our competitors, either alone or with their collaboration partners, may have significantly greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing, and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors. These competitors also compete with us in recruiting and retaining qualified research and development and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with more established companies.

The key competitive factors affecting the success of NBTXR3 and any other product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price and the availability of reimbursement from government and other third-party payors. We must also protect our proprietary technology used in the development of our product candidates. Our commercial opportunity could be reduced if our competitors develop and commercialize products that are more effective or demonstrate a more favorable safety profile than any products that we may develop. Similarly, our commercial opportunity could be reduced if we fail to protect or to enforce our intellectual property rights successfully against third parties who infringe our patents or our licensors' patents, or if competitors design around our patent claims or our licensors' patent claims to produce competitive products, product candidates, processes and technologies that fall outside of the scope of our or our licensors' patents. Our competitors may also successfully complete applicable pre-marketing regulatory requirements for their products more rapidly than us.

The extent to which the COVID-19 pandemic and resulting deterioration of worldwide economic conditions adversely impacts our business, financial condition, and operating results will depend on future developments, which are difficult to predict.

In December 2019, a new strain of coronavirus, SARS-CoV-2, identified as the cause of coronavirus disease 2019 (COVID-19), emerged. Since then, SARS-CoV-2 and the resulting disease COVID-19 has spread to many countries, including each of the countries in which our clinical trials are planned or ongoing.

As a result of the COVID-19 pandemic, governmental authorities have implemented and are continuing to implement numerous and rapidly evolving measures to try to contain the virus, such as travel bans and restrictions, limits on gatherings, quarantines, shelter-in-place orders, and business shutdowns. In response to the COVID-19 pandemic and in accordance with governmental orders, we have also modified our business practices and implemented proactive measures to protect the health and safety of employees, including restricting employee travel, requiring remote work arrangements for non-laboratory employees, implementing social distancing and enhanced sanitary measures in our facilities, and cancelling attendance at in-person events and conferences. Many of the suppliers and service providers on whom we rely have made similar modifications. There is no certainty that such measures will be sufficient to mitigate the risks posed by, or the impacts and disruptions of, the COVID-19 pandemic.

As a result of the COVID-19 pandemic, we have experienced, and expect to continue to experience, disruptions and adverse impacts to our business, including delays in certain clinical trial activities. Although the ultimate impact of the COVID-19 pandemic on our business is not determinable at this stage, the operational and functional impacts of the COVID-19 pandemic could be material, including:

- Disruptions, interruptions or delays of our clinical trial activities, whether conducted by us or in collaboration with our partners (such as MD Anderson), due in particular to delays or difficulties in recruiting patients, challenges from quarantines, site closures, supply chain interruptions, limitations or redirection of human or material resources normally allocated to these clinical trials, interruptions in data collection, monitoring and/or processing, more limited access to physicians, delays in receiving, or shortages of, the supplies and materials necessary for the performance of clinical trials, or travel restrictions imposed or recommended by local authorities;
- Changes in local regulations due to the measures taken in response to the COVID-19 pandemic, which could require us to modify the conditions of our clinical trials, potentially resulting in unforeseen costs or the interruption of our trials;
- Delays in obtaining from regulatory authorities the approvals required to launch our contemplated clinical trials, as well as delays in the necessary interactions with local authorities or other important organizations and third-party partners;
- Overall reduced operational productivity, including interruptions to our research and development activity, resulting from challenges associated with remote work arrangements and limited resources available to employees working remotely; or
- Challenges in accessing, in a timely manner or on acceptable terms, financing opportunities as a result of dislocations in the capital markets, liquidity constraints on potential commercial partners, and general disruptions to global and regional economies.

While recruitment and monitoring in our clinical trials have slowed due to the pandemic and based on current circumstances, we expect that the receipt and reporting of data in head and neck cancer and immuno-oncology ("I-O") clinical trials that were underway prior to the pandemic will generally proceed as planned based on the number of patients that had already been recruited. We anticipate that, as a result of the disruptions of the COVID-19 pandemic, protocol development and review processes and enrollment in trials not yet in progress are likely to be

delayed or to progress more slowly than originally anticipated. Moreover, given recruitment barriers, we expect delays in launching these trials even after regulatory clearance to proceed is obtained.

The degree to which COVID-19 ultimately impacts our business will depend on future developments, which are highly uncertain and cannot be predicted, including, but not limited to, the severity, duration and geographic spread of the outbreak, potential resurgence events and the emergence of additional variant strains, the effectiveness of available vaccines (including with respect to emerging variants of COVID-19) and the effective distribution thereof, as well as the global, national and regional actions to contain the virus and address its impact. The resumption of normal business operations after interruptions caused by COVID-19 may be delayed or constrained by lingering effects of COVID-19 on us or our suppliers and third-party service providers, respectively. Even after the COVID-19 outbreak has subsided, we may experience material and adverse impacts as a result of the global economic impact of the COVID-19 outbreak.

The impact of COVID-19 may also exacerbate other risks discussed in this Annual Report, any of which could have a material effect on us. This situation is changing rapidly and additional impacts may arise that we are not aware of currently.

Due to our limited resources and access to capital, our decisions to prioritize development of certain product candidates or certain indications to pursue with the product candidates that we are developing may adversely affect our business prospects.

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each. In addition, for product candidates under development, such as NBTXR3, we must decide for which indications we intend to develop the product candidate for treatment. As such, we are currently primarily focused on the development of NBTXR3, particularly for the treatment of patients with locally advanced head and neck cancers, while also evaluating other indications and building out a
robust immuno-oncology program. Our decisions concerning the allocation of research, collaboration, management and financial resources toward particular product candidates, oncological indications or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from other more promising opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties with respect to some of our product development programs may also prove not to be optimal and could cause us to miss valuable opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights. If we make incorrect determinations regarding the market potential of our product candidates or misread trends in the field of cancer treatment, our business prospects could be harmed.

We will require additional funding, which may not be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

The process of developing our product candidates is expensive, lengthy and risky. We expect our research and development expenses to increase substantially as we continue to develop NBTXR3 through our clinical development programs and identify new product candidates for development. Further, as a result of our increasing commercialization efforts with respect to NBTXR3 and the costs of operating as a U.S. public company, our selling, general and administrative expenses will increase significantly in the next several years.

As of December 31, 2021, we had cash and cash equivalents of €83.9 million. We believe our cash and cash equivalents will be sufficient to fund our operations through the second quarter of 2023. However, in order to continue our ongoing research and development efforts, pursue regulatory approval and certification, and advance our commercialization efforts, we will require substantial additional funding. Also, our operating plan, including our product candidate development plans, may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other strategic alliances and licensing arrangements, or a combination of these approaches.

To the extent that we raise additional capital through the sale of additional equity or convertible securities, holders of our ordinary shares and ADSs will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our shareholders. Debt financing, if available, would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness. In addition, debt financing may involve agreements that include restrictive covenants that impose operating restrictions, such as restrictions on the incurrence of additional debt, the making of certain capital expenditures or the declaration of dividends. To the extent that we raise additional funds through arrangements with research and development partners or otherwise, we may be required to relinquish some of our technologies, product candidates or revenue streams, license our technologies or product candidates on unfavorable terms, or otherwise agree to terms unfavorable to us. Any additional fundraising efforts may divert our management’s attention from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates.

In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of specific strategic considerations.

If we are unable to obtain funding on a timely basis, our growth prospects could be impaired, the price of our ordinary shares and ADSs may decline, and we may be required to, among other things:

- delay or reduce the number or extent of our preclinical and clinical trials or eliminate them entirely;
- grant licenses to our technology to collaborative partners or third parties; or
- enter into new collaboration agreements upon less favorable conditions than we would have been able to obtain under different circumstances.

Covenants in the Finance Contract governing the EIB loan impose restrictions on the operation of our business.

The Finance Contract governing our loan from the European Investment Bank, or EIB (the "EIB loan"), contains covenants that impose restrictions on the operation of our business. For example, without the approval of the EIB, the restrictions in the Finance Contract limit our and our subsidiaries' ability, among other things, to:

- dispose of any part of our business or assets outside of arm's-length ordinary course transactions;
- restructure or make substantial changes to the nature of our business;
- enter into certain merger or consolidation transactions;
- dispose of our shareholdings in our material subsidiaries;
- pursue acquisitions or investments;
- incur any indebtedness in excess of €1.0 million in the aggregate;
- provide guarantees in respect of liabilities or other obligations;
- engage in certain hedging activities;
- grant security over our assets;
- pay dividends or repurchase our shares; and
- impair our intellectual property rights.

As a result of these covenants and restrictions, we are limited in how we conduct our business. Although the restrictions in the Finance Contract contain several exceptions and carve-outs and may be waived by EIB, as a result of the restrictions we may be unable to raise additional financing or pursue new business opportunities that we believe would be beneficial to our business objectives.

Risks Related to the Development of Our Product Candidates

Our product candidates must undergo clinical trials that are time-consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure. If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

In order to obtain requisite regulatory approvals and to successfully complete the necessary conformity assessment procedures, as applicable, we conduct preclinical and clinical programs for our product candidates with the goal of ultimately marketing therapeutic solutions to transform cancer treatments that utilize radiotherapy. NBTXR3, our lead product candidate, is currently being evaluated in a total of eight clinical trials worldwide as a potential treatment in various cancer indications. In January 2019 we announced a collaboration with MD Anderson which provides for approximately 340 patients to be enrolled across multiple clinical trials to be conducted in the United States to evaluate NBTXR3 across several cancer types. Because we are conducting clinical trials for NBTXR3 in multiple cancer indications, an unfavorable outcome in one or more trials may call into question the safety or efficacy in trials with respect to other cancer indications, and potentially undermine the validity of our nanotechnology platform.

Further, preclinical testing and clinical trials are long, expensive and unpredictable processes that can encounter extensive delays. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. For example, one patient who participated in our clinical trial evaluating NBTXR3 in patients with late-stage cancers died from his cancer before any observation of response to treatment. Although this death was determined to be unrelated to the treatment, such setbacks could cause delays in our clinical trials. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a product candidate, and delays or failure can occur at any stage. The design of a clinical trial can determine whether its results will support approval and certification of a product, as applicable, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. An unfavorable outcome in one or more trials would be a major setback for our product candidates and for us. Due to our limited financial resources, an unfavorable outcome in one or more trials may require us to delay, reduce the scope of, or eliminate one or more product development programs, which could have a material adverse effect on our business and financial condition and on the value of our ordinary shares or ADSs.

In connection with clinical testing and trials, we face a number of risks, including risks that:

- a product candidate is ineffective, inferior to existing approved treatments, unacceptably toxic, or has unacceptable side effects (both immediate or long-term);
- patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- extension studies on long-term tolerance could invalidate the use of our product;
- the results may not confirm the positive results of earlier testing or trials;
- the independent data monitoring committee assigned to review our testing and trials could identify potential flaws in, or recommend against advancement of or adjustments to, any particular trial or trial design; and
- the results may not meet the level of statistical significance required by the FDA or other regulatory agencies to establish the safety and efficacy of our product candidates.

The results of preclinical studies do not necessarily predict clinical success, and larger and later-stage clinical trials may not produce the same results as earlier-stage clinical trials. To date, clinical trials of NBTXR3 in certain oncological indications have generated favorable data; however, we may have different enrollment criteria in our future clinical trials and certain clinical trials have only yielded preliminary data. As a result, we may not observe similar results as in our prior clinical trials or in our preliminary data. Frequently, product candidates developed by pharmaceutical, biopharmaceutical and nanomedicine companies have shown promising results in preclinical studies or early clinical trials, but have subsequently suffered significant setbacks or failed in later clinical trials. Further, clinical trials of potential products often reveal that it is not possible or practical to continue development efforts for these product candidates.

We cannot guarantee that our current or future product development efforts will be successful, or completed within our anticipated time frames. If we do not successfully complete preclinical and clinical development, we will be unable to pursue required market authorization to market and sell our product candidates and generate revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before submitting marketing applications to the FDA, or initiating necessary conformity assessment procedures, as applicable. Although there are a large number of drugs and medical devices in development in Europe, the United States and other countries, only a small percentage result in the submission of a marketing application or the initiation of a conformity assessment procedure, even fewer are approved for commercialization, and only a small number achieve widespread physician and consumer acceptance following regulatory approval or successful completion of the conformity assessment procedure, as applicable. If our clinical trials are substantially delayed or fail to prove the safety and effectiveness of our product candidates in development, we may not successfully complete applicable pre-marketing regulatory requirements for any of these product candidates and our business and financial condition will be materially harmed.

Delays, suspensions and terminations in our clinical trials could result in increased costs to us and delay or prevent our ability to generate revenues.

Human clinical trials are very expensive, time-consuming, and difficult to design, implement and complete. Commencement of our clinical trials for our product candidates may be delayed for a variety of reasons, including delays in:

- demonstrating sufficient preclinical safety and efficacy to obtain regulatory approval to commence a clinical trial;
- validating test methods to support quality testing of the product candidate;
- manufacturing sufficient quantities of the product candidate necessary to conduct clinical trials;
- obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site;
- determining dosing and clinical trial design; and
- patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant oncological indication and the eligibility criteria for the clinical trial.

The completion of our clinical trials for our product candidates may be delayed, suspended or terminated due to a number of factors, including:

- lack of efficacy of product candidates during clinical trials;
- adverse events, safety issues or side effects relating to the product candidates or their formulation;
- unanticipated events during clinical trials requiring amendments to clinical trial designs or protocols;
- inability to raise additional capital in sufficient amounts to continue funding clinical trials or development programs;
- the need to sequence and prioritize clinical trials as opposed to conducting them concomitantly in order to conserve resources;
- our inability to enter into collaborations relating to the development and commercialization of our product candidates;
- our failure to conduct clinical trials in accordance with regulatory requirements or clinical trial protocols;
- our inability to manufacture or obtain from third parties sufficient quantities of product candidates for use in preclinical studies and clinical trials or of raw materials necessary for such manufacture;

- governmental or regulatory delays and changes in regulatory requirements or policy and guidance from regulatory authorities, including mandated changes in the scope or design of clinical trials or requests for supplemental information with respect to clinical trial results;
- delays in patient enrollment, variability in the number and types of patients available for clinical trials, and lower-than anticipated retention rates for patients in clinical trials;
- difficulty in patient monitoring and data collection due to failure of patients to maintain contact after treatment;
- varying interpretations of our data by the Notified Body, FDA and other regulatory agencies; and
- the need to identify alternative clinical trial sites to replace sites originally appointed for activation in Russia and Ukraine, which sites have been suspended in light of the Russian invasion of Ukraine that commenced in February 2022.

Many of these factors could also ultimately lead to the denial of our marketing application or the failure to complete applicable pre-marketing regulatory requirements for NBTXR3, or our other product candidates. If we experience delays, suspensions or terminations in a clinical trial, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed or such revenues could be reduced or fail to materialize.

We rely on third parties to assist in our discovery and development activities, manufacture the nanoparticles used in our product candidates, and conduct our clinical trials and perform data collection and analysis, which could hinder our product development prospects or result in costs and delays that prevent us from successfully commercializing our product candidates.

We currently, and expect to continue to, depend on collaborations with public and private research institutions, including hospitals, clinics and cancer treatment centers, to conduct some of our development activities. If we are unable to enter into research collaborations with these institutions, or if any one of these institutions fails to work efficiently with us, the research, development or marketing of our product candidates planned as part of the collaboration could be delayed or cancelled. In the event a collaboration agreement is terminated or we become unable to renew the arrangement under acceptable conditions, our discovery and development activities may also be delayed.

Further, we depend on our production method, which we developed internally, for the manufacturing of nanoparticles. Although we have trained our third-party manufacturers in the application of our production method (and seek to maintain quality control through, among other things, implementation of a monitoring system), we do not control such third-party manufacturers' implementation of our production methods. In addition, we cannot provide any assurance that such third-party manufacturers will comply with all necessary safety protocols with respect to the implementation of our production method. Any interruption in the production of nanoparticles using the production method, including due to injuries or safety concerns from the implementation thereof, could significantly compromise our product development efforts.

We rely, or may rely, on medical institutions, clinical investigators and contract collaborators to carry out our clinical trials and to perform data collection and analysis. For example, under our primary collaboration agreement, two NBTXR3 clinical trials are currently being run by MD Anderson, and MD Anderson is expected to serve, pursuant to the terms of the MD Anderson Collaboration Agreement as the sponsor for the remaining several clinical trials we expect to launch as part of this collaboration.

Our clinical trials conducted in reliance on third parties may be delayed, suspended, or terminated if:

- the third parties do not devote a sufficient amount of time or effort to our activities or otherwise fail to successfully carry out their contractual duties or to meet regulatory obligations or expected deadlines;
- we replace a third party; or
- the quality or accuracy of the data obtained by third parties is compromised due to their failure to adhere to clinical protocols, regulatory requirements, or for other reasons.

We rely on a number of third parties for the conduct of clinical trials and data collection and analysis. Third-party performance failures may increase our development costs, delay our ability to obtain regulatory approval or successfully complete pre-marketing certification procedures, and delay or prevent the commercialization of our product candidates. In addition, our third-party agreements usually contain a clause limiting such third party's liability, such that we may not be able to obtain full compensation for any losses we may incur in connection with the third party's performance failures. Ultimately, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of this responsibility. While we believe that in many cases there are alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without incurring delays or additional costs. Further, in the event of a default, bankruptcy or shutdown of, or a dispute with, a third party, we may be unable to enter into a new agreement with another third party on commercially acceptable terms.

We have entered, and may in the future enter, into collaboration agreements with third parties for the development and commercialization of our product candidates, which may affect our ability to generate revenues.

We have limited capabilities for product development and may seek to enter into collaborations with third parties for the development and potential commercialization of our product candidates. Should we seek to collaborate with a third party with respect to a prospective development program, we may not be able to locate a suitable collaborator and may not be able to enter into an agreement on commercially reasonable terms or at all. Even if we succeed in securing collaborators for the development and commercialization of our product candidates, such as our existing collaboration arrangements, we have limited control over the amount and timing that our collaborators may dedicate to the development or commercialization of our product candidates.

These collaborations pose a number of risks, including the following:

- collaborators may not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as budget limitations, lack of human resources, or a change in strategic focus;
- collaborators may believe our intellectual property is not valid or is unenforceable or the product candidate infringes on the intellectual property rights of others;
- collaborators may dispute their responsibility to conduct development and commercialization activities pursuant to the applicable collaboration, including the payment of related costs or the division of any revenues;
- collaborators may decide to pursue a competitive product developed outside of the collaboration arrangement;
- collaborators may not be able to obtain, or believe they cannot obtain, the necessary regulatory approvals or certifications; or
- collaborators may delay the development or commercialization of our product candidates in favor of developing or commercializing another party’s product candidate.

Thus, collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We also face competition in seeking out collaborators. If we are unable to secure new collaborations that achieve the collaborator’s objectives and meet our expectations, we may be unable to advance our product candidates and may not generate meaningful revenues.

If current or future collaboration partners do not fulfill their obligations, this may cause delays in, or discontinuation of, partner-sponsored clinical trials, reduced revenue potential, and potentially litigation.

Our collaboration agreements, and those we may enter into in the future, generally require that our collaboration partners use commercially reasonable efforts to advance the development and/or potential commercialization of our product candidates for certain indications and in specified geographies, typically in accordance with a jointly approved development plan. Such collaboration agreements generally include dispute resolution procedures, which permit both us and our collaboration partners to terminate the collaboration under certain circumstances, including upon any uncured material breach of the agreement. The failure of any collaboration partner to fulfill its obligations under a collaboration agreement may result in delays in clinical trial activities or the discontinuation of clinical trials sponsored and conducted by our collaboration partner, which could limit the geographies in which we are able to effectively develop and commercialize our product candidates.

Early termination of any collaboration agreement could result in additional costs and the loss of potential revenue opportunities. For example, in March 2021, in light of disagreements over a number of issues with respect to the development of NBTXR3 in the Asia-Pacific region, we and PharmaEngine mutually agreed to terminate the License and Collaboration agreement that we entered into in August 2012. While we will retain all rights to the development and commercialization of NBTXR3 in the Asia Pacific region, pursuant to a Termination and Release Agreement, we agreed to make payments to PharmaEngine of up to $5 million in total upfront payments upon the completion of various administrative steps in connection with the winding-up of the collaboration, $7.5 million in future payments upon a second regulatory approval of NBTXR3 in any jurisdiction of the world for any indication and to pay royalties to PharmaEngine at low-single digit royalty rates with respect to sales of NBTXR3 in the Asia-Pacific region for a 10-year period commencing on the corresponding first date of sales in the region. In addition, unilateral early termination of any collaboration agreement could result in disputes over intellectual property rights, responsibility for incurred costs or rights with respect to future revenue, which could lead to arbitration, litigation or other dispute resolution mechanisms. Disputes or litigation involving a collaboration partner may make it difficult for us to enter into a new agreement with another third party on commercially acceptable terms.

Risks Related to Obtaining Regulatory Approval or Certification for Our Product Candidates

Our business is governed by a rigorous, complex and evolving regulatory framework.

The development and commercialization of therapeutic solutions for cancer treatment are governed by a rigorous, complex and evolving global regulatory environment. Regulatory authorities, including the FDA in the United States, have imposed stringent requirements on the amount and types of data required to demonstrate the safety and efficacy of products prior to marketing and sale. Moreover, any products approved for commercialization are reassessed in terms of their patient risk/benefit ratio on a regular basis following initial approval or certification. The late discovery of issues or potential problems which were not detected during development and clinical trials can result in restrictions on sale, the suspension or withdrawal of the product from the market and an increased risk of litigation. Given that extensive global regulation has increased the cost of obtaining and maintaining the necessary marketing authorizations and the cost of successfully completing the necessary conformity assessment procedures, for therapeutic oncology solutions, and therefore may limit the economic value of a new product, the prospects for growth in this field, and for our product candidates, have been reduced.

In addition, clinical studies for our product candidates are subject to prior submission requirements to the relevant regulatory authorities of the countries in which the studies will be carried out. For example, in the United States, a clinical study may proceed once the FDA notifies the applicant that the study may proceed or after 30 days if the submission is not placed on hold by the FDA. A negative opinion from such a regulatory authority with respect to any of our clinical development programs could suspend or terminate such programs. Moreover, depending on the information provided to regulatory authorities during a clinical trial pursuant to ongoing reporting requirements, particularly about the occurrence of undesirable side effects, the regulatory authorities could decide to prematurely suspend or terminate the clinical trial.

NBTXR3 has been classified as a “Class III medical device” in the EU and as a “drug” in the United States. Independent certification organizations (“Notified Bodies”) designated by the national EU Member States, the FDA in the United States and comparable regulatory authorities in other jurisdictions must approve or certify the conformity of, as applicable, new drug or high risk medical device candidates before they can be commercialized, marketed, promoted or sold in those jurisdictions. We must provide these regulatory authorities with data from preclinical studies and clinical trials that demonstrate that our product candidates are safe and effective for a defined indication before they can be approved or certified for commercial distribution. We must provide data to ensure the strength, quality and purity of the substance and product. We must also assure the regulatory authorities that the characteristics and performance of the clinical batches will be replicated consistently in the commercial batches.

The competent authorities of EU Member States could reconsider the classification of NBTXR3 as a medical device in the EU and decide to reclassify it as a “drug.” If our product candidates were to be classified as drugs in the EU, their clinical development would become subject to a different regulatory framework. As a result, the development and commercialization process would be longer and more costly than expected . In an effort to minimize the impact of a potential reclassification of our product candidates, we are designing our clinical development programs so as to generate clinical evidence we believe will constitute a robust scientific basis, irrespective of classification..

If our product candidates are not approved for marketing by applicable government authorities or we fail to complete other applicable pre-marketing regulatory requirements, we will be unable to commercialize them.

As of the date of this Annual Report, we are primarily focusing our development and planned commercialization efforts on the EU and the United States. Although we achieved a proof-of-concept in 2019 when we completed the regulatory process for the CE mark of NBTXR3, thereby allowing the product to be commercialized in the 27 EU countries for the treatment of locally advanced STS, we are now prioritizing the development of NBTXR3 in the United States and the EU for the treatment of head and neck cancers. We cannot assure you that NBTXR3, or any of our future product candidates, will receive approval from the FDA or any other regulatory authority, or will successfully complete conformity assessment procedures in the EU. Our April 2019 CE marking for Hensify® does not provide any assurance that additional NBTXR3 product candidates will successfully complete similar regulatory procedures. Even if we successfully complete applicable pre-marketing regulatory requirements for any of our product candidates in a major market such as the United States or the EU, we may never obtain approval or commercialize our products in other major markets, due to varying approval procedures or otherwise, which would limit our ability to realize their full market potential.

Several factors will determine whether we receive FDA approval or whether we successfully complete the conformity assessment procedures in the EU, including, but not limited to:

- our ability to continue to develop our product candidates currently in preliminary clinical phases and to move our products currently in preclinical development phase to a clinical phase or from one clinical phase to the next;
- our ability, or the ability of a contracted third party, to successfully complete the clinical trials required by the set deadlines and with the human, technical and financial resources initially planned.

In the event that we do not successfully complete applicable pre-marketing regulatory requirements for our product candidates established by the applicable authorities or bodies in our target jurisdictions, we will be unable to commercialize such candidates.

Government restrictions on pricing and reimbursement, as well as other healthcare payor cost-containment initiatives, may negatively impact our ability to generate revenues even if we successfully complete applicable pre-marketing regulatory requirements to market a product.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government health administration authorities, private health insurers, health maintenance organizations and other organizations. Third-party payors determine which therapeutic treatments they will cover and establish reimbursement levels. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products and the treatment associated with use of our products. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Third-party payors are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular therapeutic treatments. Increasingly, third-party payors are requiring that healthcare companies provide them with predetermined discounts from list prices as a condition of coverage, are deploying various techniques to leverage greater discounts in competitive classes, and are challenging the prices charged for therapeutic products. In addition, in the United States, federal programs impose penalties on drug manufacturers in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor and product to product. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

The continuing efforts of third-party payors to contain or reduce costs of healthcare may negatively affect our commercialization prospects, including:

- our ability to set a price we believe is fair for our products, if approved;
- our ability to obtain and maintain market acceptance by the medical community and patients;
- our ability to generate revenues and achieve profitability; and
- the availability of capital.

We cannot be sure that coverage and reimbursement will be available for any potential product candidate that we may commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we successfully complete applicable pre-marketing regulatory requirements. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we successfully complete applicable pre-marketing regulatory requirements.

In the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “ACA”) has significantly impacted, and will continue to impact, the provision of, and payment for, healthcare. Various provisions of the ACA were designed to expand Medicaid eligibility, subsidize insurance premiums, provide incentives for businesses to provide healthcare benefits, prohibit denials of coverage due to pre-existing conditions, establish health insurance exchanges, and provide additional support for medical research. With regard to therapeutic products specifically, the ACA, among other things, expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare prescription drug benefit.

Since its enactment there have been multiple challenges to certain aspects of the ACA and considerable uncertainty remains regarding the implementation and impact of the ACA. For example, tax reform legislation was enacted at the end of 2017 that eliminated the individual mandate—a tax penalty for individuals who did not maintain mandated health insurance coverage—beginning in 2019.

In addition to further legal review of the ACA, U.S. federal and state governments are continuing to focus on the cost of health coverage, health care and pharmaceuticals although future policy or the timing of any changes remains unclear, creating significant risks for the sector. At the federal level, legislation like the Bipartisan Budget Act of 2018 (“BBA”) amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, and also increased in 2019 the percentage by which a drug manufacturer must discount the cost of prescription drugs from 50 percent to 70 percent.

In addition, both the Budget Control Act of 2011 and the American Taxpayer Relief Act of 2012 (the “ATRA”), have instituted, among other things, mandatory reductions in Medicare payments to certain providers.We cannot predict the ultimate content, timing or effect of any changes to the ACA or other federal and state reform efforts, and there

can be no assurance that any such health care reforms will not adversely affect our future business and financial results.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. Federal regulatory reform intended to reduce costs of drugs furnished under Medicare and Medicare Advantage plans through utilization management tools, like step therapy, and to increase price transparency for such drugs through the prohibition of gag clauses in pharmacy contracts became effective on January 1, 2020. Since 2017, multiple states enacted and even more states have considered proposed legislation which will require price transparency and reporting of certain manufacturer information. This trend is anticipated to continue, where legislation is expected regarding pricing transparency, marketing, access to drugs and other measures related to pricing.

In November 2020, the U.S. Department of Health and Human Services, Office of Inspector General, finalized proposed modifications to the U.S. federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, will affect discounts paid by manufacturers to Medicare Part D plans and pharmacy benefit managers working with these organizations. The rule was challenged as arbitrary and capricious under the Administrative Procedure Act. In response, the government agreed to delay the effective date and evaluate the rule adopted by the previous administration. In the interim, the status quo has been restored. In addition to these, new legislative and/or administrative measures and other initiatives to control drug costs could harm our ability to market any product candidates and generate revenues.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product candidate. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. Additionally, the United States market has been further consolidated by key private payor organizations. For instance, CVS-Aetna and Cigna-ESI mergers highlight the role of integrated payor arrangements, including PBMs, which impacts product access and affordability. Such market consolidation may further impact market pricing in the future (three PBMs now cover over 75% of the market resulting in significant negotiating power for commercial and Medicare Part D plans). Both government and commercial payors are aggressively pursuing and implementing cost containment tools designed to lower plan-level net costs. Further, the United States Congress is expected to continue its focus on pharmaceutical pricing with bipartisan support. Additional legislative focus from state and federal bodies is anticipated. The potential implementation of further pricing practice scrutiny and related cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products. Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future.

In some foreign countries, the proposed pricing for a therapeutic product must be approved before it may be lawfully marketed. In addition, in some foreign markets, the pricing of therapeutic products is subject to government control and reimbursement may in some cases be unavailable. The requirements governing pricing of therapeutic products vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of therapeutic products for which their national health insurance systems provide reimbursement and to control the prices of therapeutic products for human use. A Member State may approve a specific price for the therapeutic product, may refuse to reimburse a product at the price set by the manufacturer or may instead adopt a system of direct or indirect controls on the profitability of the company placing the therapeutic product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for therapeutic products will allow favorable reimbursement and pricing arrangements for NBTXR3 or any of our other product candidates that may be approved.

Historically, therapeutic products launched in the EU do not follow price structures of the United States and generally tend to have significantly lower prices.

The scope and nature of pricing controls vary country to country, but common themes include the following: reference pricing, systematic price reduction, formularies, volume limitations, patient copayment limitations, and generic substitution. In the United States and internationally, we believe that pricing pressures at multiple levels of government, including third party review of pricing practices, will continue and may increase, which may make it difficult for us to sell our potential product candidates that may be approved in the future at a price acceptable to us or any third parties with whom we may choose to collaborate.

Even if we successfully complete applicable pre-marketing regulatory requirements for the commercialization of our product candidates, the terms of approvals or certifications and ongoing regulation of our products may limit how we market our products, which could materially impair our ability to generate revenues.

Even if we successfully complete applicable pre-marketing regulatory requirements for the commercialization of a product candidate, the resulting approval or certification may carry conditions that limit the market for the product or put the product at a competitive disadvantage relative to alternative therapies. For instance, a regulatory approval may limit the indicated uses for which we can market a product or the patient population that may utilize the product.

These restrictions could make it more difficult to market the product effectively. Accordingly, assuming we successfully complete applicable pre-marketing regulatory requirements for the commercialization of any of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance.

A Fast Track designation by the FDA may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive regulatory approval.

In February 2020, the FDA granted Fast Track designation for NBTXR3 activated by radiation therapy, with or without cetuximab, for the treatment of patients with locally advanced head and neck squamous cell cancer who are not eligible for platinum-based chemotherapy. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for that condition, the product sponsor may apply for FDA Fast Track designation. The FDA has broad discretion whether or not to grant this designation. Even though we have received Fast Track designation for NBTXR3, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw a Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Many products that have received Fast Track designation have failed to obtain approval from the FDA.

A Breakthrough Therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive regulatory approval.

We do not currently have Breakthrough Therapy designation for any of our product candidates but may seek it in the future. A Breakthrough Therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for development.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe, after completing early clinical trials, that one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead decide not to grant that designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as Breakthrough Therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

Risks Related to the Production and Manufacturing of Our Product Candidates

We may not have access to the raw materials and other components necessary for the manufacturing of our product candidates.

We are dependent on third parties for the supply of various materials that are necessary to produce our product candidates for clinical trials. See “Item 4B. Business Overview—Manufacturing.” Although we have entered into agreements related to the supply of the raw materials used in the manufacturing of our nanoparticles, the supply could be reduced or interrupted at any time. In such case, we may not be able to find other suppliers of acceptable materials in appropriate quantities at an acceptable cost. If we lose key suppliers or the supply of materials is diminished or discontinued, or in the event of a major or international crisis impacting mining or the extraction of minerals in certain regions, we may not be able to continue to develop, manufacture and market our product candidates or products in a timely and competitive manner. In addition, these materials are subject to stringent manufacturing processes and rigorous testing. Delays in the completion and validation of facilities and manufacturing processes of these materials could adversely affect our ability to complete trials and commercialize our products in a cost-effective and timely manner. If we encounter difficulties in the supply of these materials, chemicals or other necessary products, or if we were not able to maintain our supply agreements or establish new supply agreements in the future, or incur increased production costs as a result of any of the foregoing, our product development and our business prospects could be significantly compromised.

In November 2017, we opened a new facility to expand our manufacturing capabilities, increase production capacity of NBTXR3 for our clinical trial needs and prepare for potential commercialization. This new facility is located in the Villejuif BioPark, a scientific research and innovation center just outside of Paris, France. We expect that the facility will expand in due course our production capacity with the aim to produce NBTXR3 for our ongoing clinical trials and our initial commercial phase. However, we have not yet manufactured significant doses of NBTXR3 at this scale and may never be successful in developing manufacturing capabilities sufficient to meet our clinical trial needs. Moreover, we may have more limited access to raw materials and other components necessary for the manufacturing of our product candidates than third-party manufacturers, who may have more established relationships with suppliers, greater financial resources than us, and/or the ability to leverage purchasing scale for more efficient pricing of raw materials. Our manufacturing facilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures, regulatory issues and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

Our manufacturing facilities as well as our subcontractor's manufacturing facilities are subject to significant government regulations and approvals. If we or our third-party manufacturers fail to comply with these regulations or maintain these approvals, our business will be materially harmed.

We contract the production of NBTXR3 for use in clinical trials to high-precision manufacturing partners. In addition, in 2017 we expanded our own manufacturing capabilities by opening an internal research and innovation center facility just outside of Paris, France. We and our third-party manufacturers are subject to ongoing regulation and periodic inspection by the national competent authorities of the EU Member States, FDA and other regulatory bodies to ensure current Good Manufacturing Practices ("cGMP") and international organization for standards ("ISO") compliance, as applicable. Any failure to follow and document our or their adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical trials, may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of marketing applications or the completion of pre-marketing certification procedures, as applicable, for our products.
Failure to comply with applicable regulations could also result in the FDA or other applicable regulatory authorities taking, or causing to be taken, various actions, including:

- levying fines and other civil penalties;
- imposing consent decrees or injunctions;
- requiring us to suspend or put on hold one or more of our clinical trials;
- suspending or withdrawing regulatory approvals or certifications;
- delaying or refusing to approve pending applications or supplements to approved applications;
- requiring us to suspend manufacturing activities or product sales, imports or exports;
- requiring us to communicate with physicians, hospitals and other stakeholders about concerns related to actual or potential safety, efficacy, and other issues involving our products;
- ordering or requiring product recalls or seizing products;
- imposing operating restrictions; and
- seeking criminal prosecutions.

Any of the foregoing actions could be detrimental to our reputation, business, financial condition or operating results. Furthermore, our key suppliers may not continue to be in compliance with all applicable regulatory requirements, which could result in our failure to produce our products on a timely basis and in the required quantities, if at all. In addition, before any products would be considered for marketing in the United States, the EU or elsewhere, our suppliers will have to pass an audit by the applicable regulatory agencies. We are dependent on our suppliers' cooperation and ability to pass such audits, and the audits and any audit remediation may be costly. Failure to pass such audits by us or any of our suppliers would affect our ability to commercialize our product candidates in the United States, the EU or elsewhere.

Risks Related to the Commercialization of Our Product Candidates

The commercial success of our products is not guaranteed.

To date, we have the right to CE mark, and therefore to commercialize only one of our product candidates, Hensify®, the brand name for NBTXR3 for the treatment of locally advanced STS. This does not mean any of our other product candidates will receive approval for commercialization or that Hensify® will receive approval for commercialization in any other jurisdictions. In addition, even though we received approval for Hensify® and even if we receive additional approvals to commercialize any of our product candidates in the EU, the United States or elsewhere, we will need to gain the approval of the medical community, care prescribers and third party payors in order to achieve commercial success. Despite the fact that we have successfully completed all the regulatory steps allowing us to commercialize Hensify® in the EU, we have not yet undertaken any commercialization activities. Following evaluation of the results from Study 102 and NANORAY-312, we intend to undertake a strategic review and to determine where we believe we are best positioned to pursue commercialization, including our commercialization strategy with respect to Hensify®.

Even if the medical community accepts a product as safe and efficacious for its indicated use, physicians may choose to restrict the use of the product if we are unable to demonstrate that, based on experience, clinical data, side-effect profiles and other factors, our product is preferable to any alternative treatment methods. We cannot

predict the degree of market acceptance of any product candidate that successfully completes applicable pre-marketing regulatory requirements, which will depend on a number of factors, including, but not limited to:

- the perceived therapeutic benefit of the product by care prescribers;
- the potential occurrence of unanticipated or harmful side effects;
- the ease of integration of the product in current care/treatment processes;
- the advantages and disadvantages of the product compared to existing or alternative treatments;
- the ability of physicians to correctly and effectively administer our product to patients;
- the cost of treatment, and coverage and reimbursement policies of third-party payors, including government payors, pertaining to the product;
- our ability to educate the medical community about the safety and effectiveness of the product;
- support from the medical community in the oncology field; and
- the development of one or more competing products for the same oncological indication, including therapies with a mode of action similar to that of NBTXR3.

Even if our products are able to improve current therapeutic responses, poor market penetration, resulting from one or more of the factors listed above, could have a negative impact on our business prospects. Other product solutions which directly or indirectly compete with our products could also hinder our development efforts or render our products obsolete. Similarly, to the extent a cancer treatment method is shown to be more effective than, or were to displace, radiotherapy, our business would be adversely affected. Despite our best efforts, we cannot guarantee that the clinical development of our product candidates will result in successful completion of applicable pre-marketing regulatory requirements for commercialization, or that even if we do complete such requirements, that our products will be accepted by the market and experience commercial success.

Even if we successfully complete clinical trials of our product candidates, those candidates may not be commercialized successfully for other reasons.

Even if we successfully complete clinical trials for one or more of our product candidates and complete relevant regulatory requirements, those candidates may not be commercialized for other reasons, including:

- failing to receive regulatory clearances required to market them as drugs or medical devices, as applicable;
- being subject to proprietary rights held by others;
- failing to obtain clearance from regulatory authorities for the manufacturing of our products;
- being difficult or expensive to manufacture on a commercial scale;
- having adverse side effects that make their use less desirable;
- failing to compete effectively with products or treatments commercialized by competitors;
- failing to show that the long-term benefits of our products exceed their risks;
- changes to our overall development priorities; or
- shifting our commercialization strategy based upon our view that the market no longer supports commercialization of a particular product candidate or for a particular indication.

Any of our product candidates for which we obtain authorization for commercialization could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products following approval.

Any of our product candidates for which we successfully complete applicable pre-marketing regulatory requirements for commercialization, such as CE marking for NBTXR3 for the treatment of locally advanced STS in the EU, as well as the manufacturing processes, post-approval studies and measures, and labeling and promotional activities for such products, among other things, will be subject to continual requirements of and review by the Notified Body and national competent authorities of EU Member States, FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if we successfully complete applicable pre-marketing regulatory requirements for a product candidate, the resulting approval or certification, as applicable, may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including an FDA requirement to implement a risk evaluation and mitigation strategy to ensure that the benefits of a drug product outweigh its risks.

The FDA, and other regulatory bodies, may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product, such as long term observational studies. The FDA and other U.S. agencies, including the U.S. Department of Justice, closely regulate and monitor the post-approval marketing and promotion of therapeutic products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The national competent authorities of EU Member States and FDA impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not limit the marketing of any of our product candidates to their approved indications, we may be subject to warnings or enforcement action for off-label marketing. Similarly, we cannot promote our products before completion of applicable pre-marketing regulatory requirements. Violation of the

U.S. Federal Food, Drug and Cosmetic Act, and other related statutes, may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

If we are unable to establish sales, marketing and distribution capabilities for our product candidates, whether it be an internal infrastructure or an arrangement with a commercial partner, we may not be successful in commercializing those product candidates if and when they are approved or duly CE marked.

We do not currently have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of drug or medical device products. We are currently prioritizing the development of NBTXR3 in the United States and the EU for the treatment of head and neck cancers while also evaluating NBTXR3 in the treatment of various other indications and building out a robust immuno-oncology program. At such time as we pursue commercial sales with respect to an approved product candidate, we will have to quickly transition some of our resources and attention to marketing and developing a sales force, either internally or in coordination with strategic partners. We may enter into arrangements with partners for future marketing needs with respect to certain of our products, while also implementing our own sales and marketing organization with respect to other products. Such partners may not attain goals specified in agreements we enter into with them (including, for example, goals related to the timing of product commercialization, amount of sales and payment of milestones and royalties). There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize products on our own include:

- our inability to recruit, train, manage, motivate and retain adequate numbers of effective sales and marketing personnel;
- the failure of an adequate number of physicians to adopt any future products as part of treatment; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we were to sell, market and distribute any products that we develop ourselves.

Risks Related to Human Capital Management

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of December 31, 2021, we had 100 full-time employees and we expect to increase our number of employees and expand the scope and location of our operations. To manage our anticipated development, expansion and incurrence of additional expenses, including the development and potential commercialization of our product candidates, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Members of our management team may need to divert a disproportionate amount of their attention away from their day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

We depend on key management personnel and attracting and retaining other qualified personnel, and our business could be harmed if we lose key management personnel or cannot attract and retain other qualified personnel.

Our success depends to a significant degree upon the technical skills and continued service of certain members of our management team, particularly Laurent Levy, Ph.D., our Chairman of the Executive Board. The loss of the services of any member of our management team could have a material adverse effect on us.

Our success will also depend upon our ability to attract and retain additional qualified management, regulatory, technical, and sales and marketing executives and personnel. The failure to attract, integrate, motivate, and retain additional skilled and qualified personnel could have a material adverse effect on our business. We compete for such personnel against numerous companies, including larger, more established companies with significantly greater

financial resources than we possess. In addition, failure to succeed in our product candidates' development may make it more challenging to recruit and retain qualified personnel. There can be no assurance that we will be successful in attracting or retaining such personnel and the failure to do so could have a material adverse effect on our business, financial condition and results of operations.

Being a public company requires significant resources and management attention and may affect our ability to attract and retain executive management and qualified supervisory board members.

As a public company in both the United States and France, we incur significant legal, accounting and other compliance expenses. In the United States, we are subject to the Exchange Act, including the reporting requirements thereunder, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, certain Nasdaq corporate governance requirements and other applicable securities laws, rules and regulations. Compliance with these laws, rules and regulations will increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and increase demand on our systems and resources, particularly after we are no longer an emerging growth company.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting, and will, in the future, be required to provide an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include this attestation report on internal control over financial reporting issued by our independent registered public accounting firm. When our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of complying with Section 404 will significantly increase and management's attention may be diverted from other business concerns, which could adversely affect our business and results of operations. We may need to hire more employees in the future or engage outside consultants to comply with these requirements, which will further increase our costs and expenses. If we fail to implement the requirements of Section 404 in the required timeframe, we may be subject to sanctions or investigations by regulatory authorities, including the SEC and Nasdaq. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ADSs could decline, and we could be subject to sanctions or investigations by regulatory authorities. Failure to implement or maintain effective internal control systems required of public companies could also restrict our future access to the capital markets. In addition, enhanced legal and regulatory regimes and heightened standards relating to corporate governance and disclosure for public companies result in increased legal and financial compliance costs and make some activities more time consuming.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with legal requirements or the requirements of the CMS, national competent authorities of EU Member States, FDA and other government regulators, provide accurate information to applicable government authorities, comply with fraud and abuse and other healthcare laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could substantially disrupt our operations.

Risks Related to Operational Compliance and Risk Management

We use hazardous chemicals in our business. Any claims relating to improper handling, storage or disposal of these materials could be time-consuming and costly.

Our research and development processes involve the controlled storage, handling, use and processing of hazardous materials (notably radioactive substances), including toxins and chemical agents. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed any insurance coverage and our total assets. EU and U.S. federal, state, local or other foreign laws and regulations govern the use, manufacture, storage, handling and disposal of these hazardous materials and specified waste products, as well as the discharge of pollutants into the environment and human health and safety matters. Compliance with environmental laws and regulations may be expensive and may impair our research and development efforts. If we fail to comply with these requirements, we could incur substantial costs, including civil or criminal fines and penalties, clean-up costs or capital expenditures for control equipment or operational changes necessary to achieve and maintain compliance.

In addition, we cannot predict the impact on our business of new or amended environmental laws or regulations or any changes in the way existing and future laws and regulations are interpreted and enforced.

Product liability and other lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our product candidates.

The risk that we may be sued on product liability claims is inherent in the development and commercialization of therapeutic products. Side effects of, manufacturing defects in, or improper physician administration of, products that we develop could result in the deterioration of a patient’s condition, injury or even death. For example, our liability could be sought after by patients participating in clinical trials due to unexpected side effects resulting from the administration of our products. Once a product successfully completes applicable pre-marketing regulatory requirements and is commercialized, the likelihood of product liability lawsuits increases. Criminal or civil proceedings might be filed against us by patients, physicians, regulatory authorities, pharmaceutical companies and any other third party using or marketing our products. These actions could include claims resulting from acts by our collaboration partners, potential licensees and subcontractors, over which we have little or no control. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and may be forced to limit or forgo further commercialization of the affected products. Any such adverse outcomes in future legal proceedings could also damage our market reputation which could in turn have an adverse effect on our ability to commercialize our products successfully.

We maintain product liability insurance coverage for our clinical trials at levels which we believe are appropriate for our clinical trials. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. In addition, in the future, we may not be able to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product or other legal or administrative liability claims by us or our collaboration partners, licensees or subcontractors, which could prevent or inhibit the commercial production and sale of any of our product candidates that complete applicable pre-marketing regulatory requirements.

We are subject to healthcare laws and regulations which may require substantial compliance efforts and could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings, among other penalties.

Healthcare providers, physicians and others will play a primary role in the recommendation, and the incorporation into treatment regimes, of our products, if approved and duly CE-marked. Our business operations in the United States and our arrangements with clinical investigators, healthcare providers, consultants, third-party payors and patients expose us to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, our research, proposed sales, marketing and education programs of our product candidates that successfully complete applicable pre-marketing regulatory requirements. Restrictions under applicable U.S. federal, state and foreign healthcare laws and regulations include, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and wilfully soliciting, offering, receiving or providing remuneration, including any kickback, bribe or rebate, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any item, good, facility or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- U.S. federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which can be enforced by individuals through civil whistleblower or qui tam actions, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which created additional federal criminal statutes which prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or knowingly and willingly falsifying, concealing or covering up a material fact or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, which impose certain requirements on covered entities, including certain healthcare providers, health plans and healthcare clearing houses, and their business associates, individuals and entities that perform functions or activities that involve individually identifiable health information on behalf of covered entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the laws and regulations relating to the protection of personal data, and in particular Regulation (EU) 2016/679 of April 27, 2016, or the General Data Protection Regulation (“GDPR”), which imposes strict requirements on activities that involve the processing of “personal data” (i.e., any information relating to an identified or identifiable natural person), as well as any national implementing law. For example, the GDPR requires the following non-exhaustive requirements: data processing activities must be justified by a legal basis, data subjects must be informed of the characteristics of the processing of their personal data, adequate security measures must be implemented, contractual relationships with data processors and transfers of personal data outside of the EU must be formalized and performed in compliance with data protection rules, data controllers must hold and maintain up to date records of data processing activities, data privacy impact assessments must be performed under certain circumstances, and personal data breaches must be notified. In 2019, a GDPR gap analysis was carried out by external experts on our behalf and we are in the process of implementing the most critical actions suggested to us to be taken;
- U.S. federal transparency requirements under the Physician Payments Sunshine Act, enacted as part of the ACA, that require applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program, with specific exceptions, to track and annually report to CMS payments and other transfers of value provided to physicians and teaching hospitals, and certain ownership and investment interests held by physicians or their immediate family members; and
- analogous state or foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements, state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could substantially disrupt our operations. If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Risks Related to Intellectual Property

Our ability to compete may decline if we do not adequately protect our intellectual property proprietary rights.

Our commercial success depends, in part, on obtaining and maintaining proprietary rights to our and our licensors' intellectual property as well as successfully defending these rights against third-party challenges. We will only be able to protect our products, product candidates, processes and technologies from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. Our ability to obtain patent protection for our products, product candidates, processes and technologies is uncertain due to a number of factors, including:

- we or our licensors may not have been the first to invent the technology covered by our or their pending patent applications or issued patents;
- we cannot be certain that we or our licensors were the first to file patent applications covering our products, product candidates, processes or technologies, as patent applications in the United States and most other countries are confidential for a period of time after filing;
- others may independently develop identical, similar or alternative products, product candidates, processes and technologies;
- the disclosures in our patent applications or our licensors' patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our pending patent applications or our licensors' pending patent applications may not result in issued patents;
- we or our licensors may not seek or obtain patent protection in countries or jurisdictions that may eventually provide us a significant business opportunity;
- any patents issued to us or our licensors may not provide a basis for commercially viable products, product candidates, processes and technologies, may not provide any competitive advantages, or may be successfully challenged by third parties, which may result in our patent claims or our licensors' patent claims being narrowed, invalidated or held unenforceable;
- our or our licensors' products, product candidates, processes and technologies may not be patentable;
- others may design around our patent claims or our licensors' patent claims to produce competitive products, product candidates, processes and technologies that fall outside of the scope of our patents or our licensors' patents;
- others may identify prior art or other bases upon which to challenge and ultimately invalidate our or our licensors' patents or otherwise render them unenforceable; and
- our employees may claim intellectual property rights over, or demand remuneration with respect to, inventions they helped to develop.

Even if we have or obtain patents covering our products, product candidates, processes and technologies, we may still be barred from making, using and selling our products, product candidates, processes and technologies because of the patent rights of others. Others may have filed, and in the future may file, patent applications covering products, product candidates, processes or technologies that are similar or identical to ours. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the cancer treatment field in which we are developing products.

These could materially affect our ability to develop and commercialize our product candidates or sell our products if approved. Because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that our products, product candidates, processes or technologies may infringe. These patent applications may have priority over patent applications filed by us or our licensors. Patent applications in France are only published 18 months after their priority date. In the United States, some patent applications are not published until the grant of the patent itself.

Obtaining and maintaining a patent portfolio entails significant expense and resources. Part of the expense includes periodic maintenance fees, renewal fees, annuity fees, various other governmental fees on patents and/or applications due over the course of several stages over the lifetime of patents and/or applications, as well as the cost associated with complying with numerous procedural provisions during the patent application process. We or our licensors may or may not choose to pursue or maintain protection for particular inventions. In addition, there are situations in which failure to make certain payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we choose to forgo patent protection or allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer.

Legal actions to enforce our patent rights can be expensive and may involve the diversion of significant management time. In addition, these legal actions could be unsuccessful and could also result in the invalidation of our patents or a finding that they are unenforceable. We may or may not choose to pursue litigation or other actions against those that have infringed on our patents, or used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to protect or to enforce our intellectual property rights successfully, our competitive position could suffer, which could harm our results of operations.

In addition to patent protection, because we operate in the highly technical field of the development of therapies using nanotechnology, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. We enter into non-disclosure agreements with our employees, consultants, outside collaborators, sponsored researchers and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may be breached or held unenforceable and may not effectively assign intellectual property rights to us. In particular, such parties may enter into other agreements with third parties and we would have no control over such contractual relationships and how they protect our confidential information.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not provide adequate protection for our proprietary information. For example, our security measures may not prevent an employee or consultant with authorized access from misappropriating our trade secrets and providing them to a competitor, and the recourse we have available against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets.

Furthermore, our proprietary information may be independently developed by others in a manner that could prevent legal recourse by us.

If any of our confidential or proprietary information, including our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed and our business could be materially and adversely affected.

Patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our competitive position.

The patent positions of companies developing oncology therapeutic solutions, including pharmaceutical and nanomedicine companies and other actors in our fields of business, can be highly uncertain and typically involve complex scientific, legal and factual analyses. In particular, the interpretation and breadth of claims allowed in some patents covering therapeutic compositions may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of the United States Patent and Trademark Office (the "USPTO") and foreign patent offices are sometimes uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated, narrowed or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings, post-grant review, *inter partes* review, or other administrative proceedings in the USPTO. Foreign patents as well may be subject to opposition or comparable proceedings in corresponding foreign patent offices. Challenges to our patents and patent applications or our licensors' patents and patent applications, if successful, may result in the denial of our patent applications or our licensors' patent applications or the loss or reduction in their scope. In addition, such interference, reexamination, post-grant review, *inter partes* review, opposition proceedings and other administrative proceedings may be costly and involve the diversion of significant management time. Accordingly, rights under any of our patents or our licensors' patents may not provide us with sufficient protection against competitive products or processes and any loss, denial or reduction in scope of any of such patents and patent applications may have a material adverse effect on our business.

Furthermore, even if not challenged, our patents and patent applications or our licensors' patents and patent applications may not adequately protect our product candidates, processes or technologies or prevent others from designing their products or technology to avoid being covered by our patent claims or our licensors' patent claims. If the breadth or strength of protection provided by the patents we own or license with respect to our products, product candidates, processes or technologies is threatened, it could dissuade companies from partnering with us to develop, and could threaten our ability to successfully commercialize, our product candidates, processes and technologies. Furthermore, for U.S. patent applications in which claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO in order to determine who was the first to invent any of the subject matter covered by such patent claims.

In addition, changes in, or different interpretations of, patent laws in the United States and other countries may permit others to use our discoveries or to develop and commercialize our products, product candidates, processes and technologies without providing any notice or compensation to us, or may limit the scope of patent protection that we or our licensors are able to obtain. The laws of some countries do not protect intellectual property rights to the

same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights.

If we or our licensors fail to obtain and maintain patent protection and trade secret protection of our products, product candidates, processes and technologies, we could lose our competitive advantage and competition we face would increase, potentially reducing revenues and having a material adverse effect on our business.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. Individual patent terms extend for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. In the United States, the natural expiration of a patent is generally 20 years after its first effective filing date. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of legal remedies in a particular country, and the validity and enforceability of the patent. If we or our licensors do not have sufficient patent life to protect our products, processes and technologies, our business and results of operations will be adversely affected.

If we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on our products, product candidates, processes and technologies in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. Competitors may use our technologies in jurisdictions where we or our licensors do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we or our licensors have patent protection, but where the ability to enforce our or our licensors' patent rights is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent such competition. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as the federal and state laws in the United States. Patent protection must be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we and our licensors may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. In addition, the legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to novel therapeutic products or techniques, and the requirements for patentability differ, in varying degrees, from country to country, and the laws of some foreign countries do not protect intellectual property rights, including trade secrets, to the same extent as federal and state laws of the United States. As a result, many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. Such issues may make it difficult for us to stop the infringement, misappropriation or other violation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities.

Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Furthermore, proceedings to enforce our licensors' and our patent rights and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our licensors' patents at risk of being invalidated or interpreted narrowly, could put our or our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded to us, if any, may not be commercially meaningful, while the damages and other remedies we may be ordered to pay such third parties may be significant. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

Accordingly, our licensors' and our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Third parties may assert ownership or commercial rights to inventions we develop or otherwise regard as our own.

Third parties may in the future make claims challenging the inventorship or ownership of our or our licensors' intellectual property. We have written agreements with collaborators that provide for the ownership of intellectual property arising from our collaborations. These agreements provide that we must negotiate certain commercial rights with such collaborators with respect to joint inventions or inventions made by our collaborators that arise from the results of the collaboration. In some instances, there may not be adequate written provisions to address clearly the resolution of intellectual property rights that may arise from a collaboration. If we cannot successfully negotiate sufficient ownership and commercial rights to the inventions that result from our use of a third-party collaborator's materials where required, or if disputes otherwise arise with respect to the intellectual property developed through a collaboration, we may be limited in our ability to capitalize on the full market potential of these inventions. In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective, or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and could interfere with our ability to capture the full commercial value of such inventions. Litigation may be necessary to resolve an ownership dispute, and if we are not successful, we may be precluded from using certain intellectual property and associated products, product candidates, processes and technologies, or may lose our rights in that intellectual property. Either outcome could have an adverse impact on our business.

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

We currently employ, and in the future may employ, individuals who were previously employed at universities or other biotechnology, pharmaceutical or nanomedicine companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or damage our reputation. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

A dispute concerning the infringement or misappropriation of our intellectual property rights or the intellectual property rights of others could be time-consuming and costly, and an unfavorable outcome could harm our business.

There is significant litigation in the fields of pharmaceutical and medical device development regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our products, product candidates, processes, technologies or activities infringe the intellectual property rights of others.

If our development activities are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented drugs or compositions. In addition, we may need to resort to litigation to enforce a patent issued to us, to protect our trade secrets, or to determine the scope and validity of third-party proprietary rights. If we initiate or threaten patent infringement litigation, such action could provoke third parties to assert claims against us or our licensors or could put our patents at risk of being

invalidated or interpreted narrowly. From time to time, we may hire scientific personnel or consultants formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any adverse ruling or perception of an adverse ruling in defending ourselves against these claims could have a negative impact on our cash position. Any legal action against us or our collaborators could lead to:

- payment of damages, potentially treble damages, if we are found to have wilfully infringed a party's patent rights;
- injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or
- us or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, if at all.

Any of these outcomes could hurt our cash position and financial condition and our ability to develop and commercialize our product candidates.

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

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

Risks Related to Ownership of Our Ordinary Shares and ADSs

The market price of our equity securities may be volatile or may decline regardless of our operating performance.

The trading price of our ADSs may fluctuate substantially. The trading price of our ADSs depends on a number of factors, including those described in this "Item 3D. Risk Factors", many of which are beyond our control. Such fluctuations in the market price and demand for our ordinary shares or ADSs may occur regardless of, and unrelated to, our actual operating performance, which may limit or prevent holders from readily selling their securities and may otherwise negatively affect the liquidity of our ordinary shares or ADSs. In addition, pharmaceutical, biotechnology and nanomedicine companies, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

We do not currently intend to pay dividends on our securities. In addition, French law may limit the amount of dividends we are able to distribute.

We have never declared or paid any cash dividends on our ordinary shares and do not currently intend to do so for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, holders of our ordinary shares are not likely to receive any dividends on such ordinary shares or ADSs for the foreseeable future, and the success of an investment in ordinary shares or ADSs will depend upon any future appreciation in its value. Consequently, investors may need to sell all or part of their holdings of ordinary shares or ADSs after price appreciation, which may never occur, as the only way to realize any future gains on their investment. There is no guarantee that the ordinary shares or ADSs will appreciate in value or even maintain the price at which our shareholders have purchased them. Investors seeking cash dividends should not purchase our ADSs or ordinary shares.

Further, under French law, the determination of whether we have been sufficiently profitable to pay dividends is made on the basis of our statutory financial statements prepared and presented in accordance with accounting standards applicable in France. In addition, payment of dividends may subject us to additional taxes under French law. See "Item 10B. Memorandum and Articles of Association" for further details on the limitations on our ability to declare and pay dividends. Therefore, we may be more restricted in our ability to declare dividends than companies not based in France.

In addition, exchange rate fluctuations may affect the amount of euros that we are able to distribute, and the amount in U.S. dollars that our shareholders receive upon the payment of cash dividends or other distributions we declare and pay in euros, if any. These factors could harm the value of the ADSs.

Future sales of ordinary shares or ADSs by existing shareholders could depress the market price of our ADSs and ordinary shares.

We believe that additional capital may be needed to continue our planned operations, including conducting our planned clinical trials, manufacturing and commercialization efforts, expanded research and development activities and costs associated with operating as a public company. Sales of additional ordinary shares or ADSs by us, or the perception that these sales could occur, could cause the market price of our ADSs to decline.

If our existing shareholders sell, or indicate an intent to sell, substantial amounts of ordinary shares or ADSs, the trading price of our ADSs and ordinary shares could decline significantly. In addition, such secondary sales may impair our ability to raise capital through the sale of additional equity securities.

As of December 31, 2021, we had 34,825,872 ordinary shares outstanding. Outstanding shares held by our affiliates, including our supervisory board members and executive board members, may be publicly sold in accordance with the requirements of Rule 144 under the Securities Act, including the volume and manner of sale requirements of that rule. All outstanding ADSs held by non-affiliates may be resold without restriction.

Holders of our ADSs may not be able to exercise their right to vote the ordinary shares underlying their ADSs.

Holders of ADSs may exercise voting rights with respect to the ordinary shares represented by the ADSs only in accordance with the provisions of the deposit agreement and not as a direct shareholder. The deposit agreement provides that, upon receipt of notice of any meeting of holders of our ordinary shares, the depositary will fix a record date for the determination of ADS holders who shall be entitled to give instructions for the exercise of voting rights. Upon timely receipt of notice from us, if we so request, the depositary shall distribute to the holders as of the record date (1) the notice of the meeting or solicitation of consent or proxy sent by us and (2) a statement as to the manner in which instructions may be given by the holders.

Holders of ADSs may instruct the depositary of their ADSs to vote the ordinary shares underlying their ADSs. Otherwise, Holders of ADSs will not be able to exercise voting rights, unless they withdraw the ordinary shares underlying the ADSs they hold. However, a holder of ADSs may not know about the meeting far enough in advance to withdraw those ordinary shares. If we ask for a holder of ADSs' instructions, the depositary, upon timely notice from us, will notify him or her of the upcoming vote and arrange to deliver our voting materials to him or her. We cannot guarantee to any holder of ADSs that he or she will receive the voting materials in time to ensure that he or she can instruct the depositary to vote his or her ordinary shares or to withdraw his or her ordinary shares so that he or she can vote them. If the depositary does not receive timely voting instructions from a holder of ADSs, it may give a proxy to a person designated by us to vote the ordinary shares underlying his or her ADSs. 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 a holder of ADSs may not be able to exercise his or her right to vote, and there may be nothing he or she can do if the ordinary shares underlying his or her ADSs are not voted as he or she requested.

Holders of ADSs will not be directly holding our ordinary shares.

A holder of ADSs will not be treated as one of our shareholders and will not have direct shareholder rights. French law governs our shareholder rights. The depositary, through the custodian or the custodian's nominee, will be the holder of the ordinary shares underlying ADSs held by holders of ADSs. Holders of ADSs will have ADS holder rights. Among other things, ADS holder rights do not provide for double voting rights, which otherwise would be available to holders of ordinary shares held in a shareholders' name for a period of at least two years. The deposit agreement among us, the depositary and holders of ADSs, and all other persons directly and indirectly holding ADSs, sets out ADS holder rights, as well as the rights and obligations of us and the depositary.

The right as a holder of ADSs to participate in any future preferential subscription rights or to elect to receive dividends in shares may be limited, which may cause dilution to the holdings of holders of ADSs.

According to French law, if we issue additional securities for cash, current shareholders will have preferential subscription rights for these securities on a pro rata basis unless they waive those rights at an extraordinary meeting of our shareholders (by a two-thirds majority vote) or individually by each shareholder. However, our ADS holders in the United States will not be entitled to exercise or sell such rights unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. In addition, the deposit agreement provides that the depositary will not make rights available to holders of ADSs in the United States unless the distribution to ADS holders of both the rights and any related securities are either registered under the Securities Act or exempted from registration under the Securities Act. Further, if we offer holders of our ordinary shares the option to receive dividends in either cash or shares, under the deposit agreement the depositary may require satisfactory assurances from us that extending the offer to holders of ADSs does not require registration of any securities under the Securities Act before making the option available to holders of ADSs. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. Accordingly, ADS holders may be unable to participate in our rights offerings or to elect to receive dividends in shares and may experience dilution in their holdings. In addition, if the depositary is

unable to sell rights that are not exercised or not distributed or if the sale is not lawful or reasonably practicable, it will allow the rights to lapse, in which case holders of our ADSs will receive no value for these rights.

Holders of ADSs in the United States may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying ordinary shares.

ADSs, which may be evidenced by American Depositary Receipts ("ADRs"), are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason subject to a holder of ADSs' right to cancel his or her ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, a holder of ADSs may not be able to cancel his or her ADSs and withdraw the underlying ordinary shares when he or she owes money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities.

We are an emerging growth company and we cannot be certain if the reduced disclosure requirements applicable to us will make our ADSs less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. As an emerging growth company, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, and exemptions from the requirements of holding a non-binding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our ADSs less attractive because we rely on these exemptions. If some investors find our ADSs less attractive as a result, there may be a less active trading market for our ADSs and the price of our ADSs may be more volatile. We intend to take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) December 31, 2025; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous three years; and (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. Once we cease to be an emerging growth company, we may continue to avail ourselves of the accommodations available to us as a foreign private issuer for so long as we qualify as such.

We previously identified a material weakness in our internal control over financial reporting. We may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal control over financial reporting, and as a result, investor confidence in us and the value of our common stock could be materially and adversely affected.

As a public company in the United States, we are required to establish and maintain internal control over financial reporting. Pursuant to Section 404(a) of the Sarbanes-Oxley Act we are required to furnish a report by our management that assesses our internal control over financial reporting as of year-end in our Annual Reports on Form 20-F, commencing with an initial report as of December 31, 2021, which is included in this Annual Report.

Prior to the issuance of our interim financial statements as of and for the six months ended June 30, 2021, a deficiency, which constituted a material weakness in our internal control over financial reporting, was identified. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. A material adjustment was made to our interim financial statements as of and for the six months ended June 30, 2021 prior to their issuance which resulted from a deficiency in the controls over the evaluation of certain contracts and the related accounting. The identified deficiency related to the timing of the recognition of expenses associated with new contracts signed with certain contract research organizations for one of our clinical trials. Specifically, we made advance payments that were recorded as expenses of the period instead of prepaid expenses (which in turn inappropriately increased the R&D expenses). Consequently, a material weakness was disclosed in connection with the reporting of our interim financial statements. This material weakness did not result in material adjustments, or restatements, of our audited consolidated financial statements or disclosures for any prior period previously reported by us.

During the year ended December 31, 2021, we remediated the identified material weakness in internal control over financial reporting identified above. Under the supervision of management and the oversight of our Audit Committee, Under supervision of management and the oversight of our Audit Committee, the Company increased its internal control personnel, strengthened the necessary skills for employees involved in internal control over financial reporting, implemented a more robust data collection system and enhanced reporting processes, including more

detailed accounting analyses at time of contract execution next to engaging independent specialists to modernize and perform certain internal control functions.

If we are unable to maintain an effective system of internal control over financial reporting, the reliability of our financial reporting, investor confidence in us and the value of our common stock could be materially and adversely affected. In addition, we may discover other control deficiencies in the future, and we cannot assure you that we will not have a material weakness in future periods.

ADSs holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiffs in any such action.

The deposit agreement governing the ADSs representing our ordinary shares provides that, to the fullest extent permitted by law, ADS holders, including holders who acquire ADSs in the secondary market, waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our shares, the ADSs or the deposit agreement, including any claim under the U.S. federal securities laws.

If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable based on the facts and circumstances of that case in accordance with the applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the United States Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, by a federal or state court in the City of New York, which has non-exclusive jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver provision, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this is the case with respect to the deposit agreement and the ADSs. It is advisable that holders of our ADSs consult legal counsel regarding the jury waiver provision before acquiring ADSs and thereby entering into the deposit agreement.

If holders of our ADSs or any other beneficial owners of ADSs bring a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, they may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and the depositary. If a lawsuit is brought against either or both of us and the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have, including results that could be less favorable to the plaintiffs in any such action.

Nevertheless, if this jury trial waiver provision is not permitted by applicable law, an action could proceed under the terms of the deposit agreement with a jury trial. No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Risks Related to Our Status as a Non-U.S. Company

The rights of shareholders in companies subject to French corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.

We are a French company with limited liability. Our corporate affairs are governed by our By-laws and by the laws governing companies incorporated in France. The rights of shareholders and the responsibilities of members of our executive board and supervisory board are in many ways different from the rights and obligations of shareholders in companies governed by the laws of U.S. jurisdictions. For example, in the performance of its duties, our executive board and supervisory board are required by French law to consider the interests of our company, its shareholders, its employees and other stakeholders, rather than solely our shareholders and/or creditors. It is possible that some of these parties will have interests that are different from, or in addition to, the interests of our shareholders or holders of ADSs.

Further, in accordance with French law, double voting rights automatically attach to each ordinary share of companies listed on a regulated market (such as the regulated market of Euronext in Paris, where our ordinary shares are listed) that is held of record in the name of the same shareholder for a period of at least two years, except as otherwise set forth in a company's by-laws. Our By-laws currently do not exclude such double voting rights. See "Item 6C—Board Practices—Corporate Governance Practices" and "Item 10B. Memorandum and Articles of Association." Ordinary shares held in the form of ADSs are not be eligible for double voting rights.

U.S. investors may have difficulty enforcing civil liabilities against our company and supervisory board and senior management and the experts named in this Annual Report.

Certain members of our executive board, supervisory board and senior management and certain experts named in this Annual Report are non-residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States. Additionally, it may be difficult to assert U.S.

securities law claims in actions originally instituted outside of the United States. Foreign courts may refuse to hear a U.S. securities law claim because foreign courts may not be the most appropriate forums in which to bring such a claim. Even if a foreign court agrees to hear a claim, it may determine that the law of the jurisdiction in which the foreign court resides, and not U.S. law, is applicable to the claim. Further, if U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process, and certain matters of procedure would still be governed by the law of the jurisdiction in which the foreign court resides. In particular, there is some doubt as to whether French courts would recognize and enforce certain civil liabilities under U.S. securities laws in original actions or judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in France. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered but is intended to punish the defendant. French law provides that a shareholder, or a group of shareholders, may initiate a legal action to seek indemnification from the directors of a corporation in the corporation's interest if it fails to bring such legal action itself. If so, any damages awarded by the court are paid to the corporation and any legal fees relating to such action may be borne by the relevant shareholder or the group of shareholders.

The enforceability of any judgment in France will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and France do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

Our By-laws and French corporate law contain provisions that may delay or discourage a takeover attempt.

Provisions contained in our By-laws and French corporate law could make it more difficult for a third party to acquire us, even if doing so might be beneficial to our shareholders. In addition, provisions of French law and our By-laws impose various procedural and other requirements, which could make it more difficult for shareholders to effect certain corporate actions. These provisions include the following:

- provisions of French law allowing the owner of 90% of the share capital or voting rights of a public company to force out the minority shareholders following a tender offer made to all shareholders are only applicable to companies listed on a regulated market or a multilateral trading facility in a Member State of the EU or in a state party of the European Economic Area Agreement, including the main French stock exchange, and will therefore be applicable to us only if we continue to dual-list in France;
- a merger (i.e., in a French law context, a stock-for-stock exchange after which our company would be dissolved without being liquidated into the acquiring entity and our shareholders would become shareholders of the acquiring entity) of our company into a company incorporated in the EU would require the approval of our executive board as well as a two-thirds majority of the votes cast by the shareholders present, represented by proxy or voting by mail at the relevant meeting;
- a merger of our Company into a company incorporated outside of the EU would require the unanimous approval of our shareholders;
- under French law, a cash merger is treated as a share purchase and would require the consent of each participating shareholder;
- our shareholders have granted and may grant in the future to our executive board broad authorizations to increase our share capital or to issue additional ordinary shares or other securities (for example, warrants) to our shareholders, the public or qualified investors, including as a possible defense following the launching of a tender offer for our shares;
- our shareholders have preferential subscription rights proportional to their shareholding in our company on the issuance by us of any additional shares or securities giving right, immediately or in the future, to new shares for cash or a set-off of cash debts, which rights may only be waived by the extraordinary shareholders' general meeting (by a two-thirds majority vote) of our shareholders or on an individual basis by each shareholder;
- our supervisory board has the right to appoint new members to fill a vacancy created by the resignation or death of a member, subject to the approval by the shareholders of such appointment at the next shareholders' meeting, which prevents shareholders from having the sole right to fill vacancies on our supervisory board;
- the members of our executive board are appointed by our supervisory board and can be removed either by our supervisory board or by the shareholders' general meeting;
- our supervisory board can only be convened by its chairman, by its vice-president, by any two members acting jointly, or, on a reasoned request (e.g. when no board meeting has been held for more than two consecutive months), by (1) members representing at least one-third of the total number of members of our supervisory board or (2) a member of the executive board;
- our supervisory board's meetings can only be regularly held if at least half of its members attend either physically or by way of videoconference or teleconference, enabling the members' identification and ensuring their effective participation in the supervisory board's decisions;
- our ordinary shares are nominative or bearer, if the legislation so permits, according to the shareholder's choice;
- under French law, (a) any non-French citizen, (b) any French citizen not residing in France, (c) any non-French entity or (d) any French entity controlled by one of the aforementioned persons or entities may have to file a declaration for statistical purposes with the Bank of France (Banque de France) within 20 business days following the date of certain direct foreign investments in us, including any purchase of our ADSs. In

particular, such filings are required in connection with investments exceeding €15,000,000 that lead to the acquisition of at least 10% of our share capital or voting rights or cross such 10% threshold. See "Item 10B. Memorandum and Articles of Association;"
- under French law, certain investments in any entity governed by French law relating to certain strategic industries (such as research and development in biotechnologies and activities relating to public health) and activities by individuals or entities not French, not resident in France or controlled by entities not French or not resident in France are subject to prior authorization of the Ministry of Economy; see "Item 10B. Memorandum and Articles of Association;"
- approval of at least a majority of the votes cast by shareholders present, represented by a proxy, or voting by mail at the relevant ordinary shareholders' general meeting is required to remove members of the supervisory board with or without cause;
- advance notice is required for nominations to the members of the supervisory board or for proposing matters to be acted upon at a shareholders' meeting, except that a vote to remove and replace a member of our supervisory board can be proposed at any shareholders' meeting without notice;
- pursuant to French law, our By-laws, including the sections relating to the number of our supervisory board's members and election and removal of a member of the supervisory board from office, may only be modified by a resolution adopted by a two-thirds majority vote of our shareholders present, represented by a proxy or voting by mail at the meeting;
- in the event where certain ownership thresholds would be crossed, a number of disclosures should be made by the relevant shareholder and can impose certain obligations; see "Item 10B. Memorandum and Articles of Association;" and
- transfers of shares shall comply with applicable insider trading rules and regulations, and in particular with the Market Abuse Directive and Regulation dated April 16, 2014.

Our business may be exposed to foreign exchange risks.

We incur some of our expenses, and may in the future derive revenues, in currencies other than the euro. In particular, as we expand our operations and continue to conduct clinical trials in the United States, we will continue to incur expenses in U.S. dollars. As a result, we may be exposed to foreign currency exchange risk as our results of operations and cash flows would be subject to fluctuations in foreign currency exchange rates. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro.

Therefore, for example, an increase in the value of the euro against the U.S. dollar could have a negative impact on our revenue and earnings growth as U.S. dollar revenue and earnings, if any, are translated into euros at a reduced value. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows. Our ADSs are quoted in U.S. dollars on the Nasdaq Global Select Market, while our ordinary shares trade in euros on the regulated market of Euronext in Paris. Our financial statements are prepared in euros. Therefore, fluctuations in the exchange rate between the euro and the U.S. dollar will also affect, among other matters, the value of our ordinary shares and ADSs.

Our international operations involve additional risks, and our exposure to these risks will increase as our business continues to expand.

We operate in a number of jurisdictions and intend to continue to expand our global presence. To date, we have focused our development and planned commercialization efforts on the EU and the United States, and to a lesser extent, Asia. International operations are subject to the legal, political, regulatory, and social requirements and economic conditions in the jurisdictions in which they are conducted. Risks inherent to international operations include, but are not limited to:

- currency exchange restrictions or costs and exchange rate fluctuations;
- exposure to local or regional economic or political instability, war or other armed conflicts, such as the Russian invasion of Ukraine that commenced in February 2022, and other threatened or actual acts of terrorism and security concerns in general;
- compliance with various laws and regulatory requirements relating to anti-corruption, antitrust or competition, economic sanctions, data content, data protection and privacy, employment and labor laws and health and safety;
- difficulties in attracting and retaining qualified employees in certain international markets, as well as managing staffing and operations due to increased complexity, distance, time zones, language and cultural differences;
- difficulty in enforcing agreements, judgments, and arbitration awards in various legal systems; and
- inability to obtain, maintain or enforce our intellectual property rights.

We believe that our overall success as a global business depends on our ability to succeed in different legal, regulatory, economic, social, and political situations and conditions. We may not be able to develop and implement effective policies and strategies in each jurisdiction where we may conduct operations or do business in the future.

As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than a U.S. company. This may limit the information available to holders of ADSs and ordinary shares.

We are a foreign private issuer, as defined in the SEC's rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to public companies organized within the United States. For example, we are exempt from certain rules under the Exchange Act that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act, including the U.S. proxy rules under Section 14 of the Exchange Act. In addition, our executive board members and supervisory board members are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, while we currently make annual and semi-annual filings with respect to our listing on the regulated market of Euronext in Paris and expect to file financial reports on an annual basis with the SEC and furnish semi-annual financial information with the SEC, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. public companies and will not be required to file quarterly reports on Form 10-Q or current report on Form 8-K under the Exchange Act. Accordingly, there will be less publicly available information concerning our company than there would be if we were not a foreign private issuer.

As a foreign private issuer, we are permitted and we expect to follow certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq's corporate governance standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with the Nasdaq corporate governance standards.

As a foreign private issuer listed on the Nasdaq Global Select Market, we will be subject to Nasdaq's corporate governance standards. However, Nasdaq rules provide that foreign private issuers are permitted to follow home country corporate governance practices in lieu of Nasdaq's corporate governance standards as long as notification is provided to Nasdaq of the intention to take advantage of such exemptions. Certain corporate governance practices in France, which is our home country, may differ significantly from Nasdaq corporate governance standards. Other than as set forth in this Annual Report, we currently intend to comply with the corporate governance listing standards of Nasdaq to the extent possible under French law. However, we may choose to change such practices to follow additional French home country practices in the future.

As a result of the accommodations for foreign private issuers, our shareholders may be afforded less protection than they otherwise would have under Nasdaq's corporate governance standards applicable to U.S. domestic issuers. For an overview of our corporate governance practices, see "Item 6C. Board Practices - Corporate Governance Practices."

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

While we currently qualify as a foreign private issuer, 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, 2022. In the future, we would lose our foreign private issuer status if we fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if more than 50% of our securities are held by U.S. residents and more than 50% of our executive board members or supervisory board members are residents or citizens of the United States, we could lose our foreign private issuer status. As of December 31, 2021, approximately 19% of our outstanding ordinary shares are held by U.S. residents.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. We would be required under current SEC rules to prepare our financial statements in accordance with U.S. GAAP, rather than IFRS, and modify certain of our policies to comply with corporate governance practices associated with U.S. domestic issuers. Such conversion of our financial statements to U.S. GAAP would involve significant time and cost. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described under "Item 6. Directors, Senior Management and Employees - C. Board Practices - Corporate Governance Practices" and exemptions from procedural requirements related to the solicitation of proxies.

Although not free from doubt, we do not believe that we were a "passive foreign investment company" ("PFIC") for U.S. federal income tax purposes for the taxable year ended December 31, 2021. However, it is not yet known whether we will be a PFIC for the taxable year ending December 31, 2022 or in subsequent taxable years. If we are determined to be a PFIC for any taxable year, there may be adverse U.S. federal income tax consequences to U.S. holders (as defined in the section of this Annual Report titled "Item 10E. Taxation—Material U.S. Federal Income Tax Considerations").

A non-U.S. corporation will be considered a PFIC for any taxable year if either (1) at least 75% of its gross income for such year is passive income or (2) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during such year) is attributable to assets that produce or are held for the production of passive income.

Passive income for this purpose generally includes, among other things, dividends, interest, rents, royalties, gains from commodities and securities transactions, and gains from assets that produce passive income. In determining whether a foreign corporation is a PFIC, a pro rata portion of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account. Although not free from doubt, we do not believe that we were a PFIC for the taxable year ended December 31, 2021. However, it is not yet known whether we will be a PFIC for the taxable year ending December 31, 2022 or in subsequent taxable years. The determination of PFIC status is fact-specific, and a separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). Our status as a PFIC depends on the composition of our income (including whether reimbursements of certain refundable research tax credits will constitute gross income for purposes of the PFIC income test) and the composition and value of our assets. The value of our assets may be determined in large part by reference to the market value of the ADSs and our ordinary shares, which may fluctuate substantially. Our status as a PFIC may also depend in part upon how quickly we utilize the cash proceeds from our U.S. Offering (and the cash proceeds from other fund-raising activities) in our business.

If we are a PFIC for any taxable year during which a U.S. holder holds ADSs, the U.S. holder may be subject to adverse tax consequences, including (1) the treatment of all or a portion of any gain on disposition as ordinary income, (2) the application of an interest charge with respect to such gain and certain dividends and (3) compliance with certain reporting requirements. Each U.S. holder is strongly urged to consult its tax advisor regarding these issues and any available elections to mitigate such tax consequences. See "Item 10E. Taxation—Material U.S. Federal Income Tax Considerations."

Investments in our securities may be subject to prior governmental authorization under the French foreign investment control regime.

Pursuant to the provisions of the French Monetary and Financial Code (code monétaire et financier), any investment by any non-French citizen, any French citizen not residing in France, any non-French entity or any French entity controlled by one of the aforementioned persons or entities that will result in the relevant investor (a) acquiring control of an entity registered in France, (b) acquiring all or part of a business line of an entity registered in France, or (c) for non-EU or non-EEA investors crossing, directly or indirectly, alone or in concert, a 25% threshold of voting rights in an entity registered in France, in each case, conducting activities in certain strategic industries, such as activities essential to protecting public health as well as biotechnology-related research and development activities, i.e. the industry in which we operate, is subject to the prior authorization of the French Ministry of Economy, which authorization may be conditioned on certain undertakings.

In the context of the ongoing COVID-19 pandemic, the Decree (*décret*) n°2020 892 dated July 22, 2020, as amended by the Decree (*décret*) n°2020-1729 dated September 28, 2020 and by the Decree (décret) n°2021-1758 dated December 22, 2021, has created a new 10% threshold of the voting rights applicable until December 31, 2022 for the non-European investments in listed companies, in addition to the 25% above-mentioned threshold for certain activities.

On November 5, 2020, the French Ministry of Economy informed us that our activities are subject to the above described foreign investment control regime. Therefore, any investor meeting the above criteria willing to acquire all or part of our business with the effect of crossing the applicable share capital thresholds set forth by the French Monetary and Financial Code will have to request this prior governmental authorization before acquiring our ordinary shares or ADSs.

We cannot guarantee that such investor will obtain the necessary authorization in due time. The authorization may also be granted subject to conditions that deter a potential purchaser. The existence of such conditions to an investment in our securities could have a negative impact on our ability to raise the funds necessary to our development. In addition, failure to comply with such measures could result in significant consequences for the investor (including the investment to be deemed null and void). Such measures could also delay or discourage a takeover attempt, and we cannot predict whether these measures will result in a lower or more volatile market price of our ADSs or ordinary shares.

For more details on the French foreign investment control regime see "Item 10B. Memorandum and Articles of Association."

General Risk Factors

We must maintain effective internal control over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could hurt our business, lessen investor confidence and depress the market price of our securities.

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a U.S. public company, the Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our disclosure controls and procedures and the effectiveness of our internal control over financial reporting at the end of each fiscal year. Pursuant to Section 404(a) of the Sarbanes-Oxley Act, we are required to furnish an annual report by our management on our internal control over financial reporting, commencing with this Annual Report for the year ended December 31, 2021. The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These stringent standards require that our audit and finance committee be advised and regularly updated on management's review of internal control over financial reporting.

Our compliance with applicable provisions of Section 404 requires that we incur substantial accounting expense and expend significant management attention and time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements. In addition, our independent registered public accounting firm will be required to attest to the effectiveness of our internal controls over financial reporting beginning with our annual report following the date on which we are no longer an emerging growth company, which may extend until December 31, 2025.

If we fail to staff our accounting and finance function adequately or maintain internal control over financial reporting adequate to meet the requirements of the Sarbanes-Oxley Act, our business and reputation may be harmed. Moreover, if we are not able to comply with the applicable requirements of Section 404 in a timely manner, we may be subject to sanctions or investigations by regulatory authorities, including the SEC and Nasdaq. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective or if deficiencies in our internal control over financial reporting that are deemed to be material weaknesses are identified, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ADSs could decline, and we could be subject to sanctions or investigations by the SEC, Nasdaq or other regulatory authorities. Failure to implement or maintain effective internal control systems required of public companies could also restrict our access to the capital markets. The occurrence of any of the foregoing would also require additional financial and management resources.

Our internal computer systems, or those of our third-party subcontractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our operations.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. If such an event were to occur and cause interruptions in our systems, it could result in a material disruption of our operations. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval, certification and commercialization efforts and significantly increase our costs to recover or reproduce the lost data. In addition, system redundancy may be ineffective or inadequate, and our disaster recovery planning may not be sufficient to cover all eventualities. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities, damage to our reputation, and the further development of our product candidates could be delayed. In addition, we may not have adequate insurance coverage to compensate for any losses associated with such events.

Use of social media by third parties may materially and adversely impact our reputation.

There has been a marked increase in the use of social media platforms and similar devices, including weblogs (blogs), social media websites and other forms of Internet-based communications which allow individual access to a broad audience of interested persons. The medical community and care prescribers may value any such readily available information concerning our products or product candidates and may act on such information without further investigation, authentication and without regard to its accuracy. Social media platforms and devices immediately publish the content their subscribers and participants post, often without filters or checks on accuracy of the content posted.

The opportunity for dissemination of information, including inaccurate information, is virtually limitless. Information concerning or affecting us, including information regarding our products, product candidates or proprietary nanotechnology, may be posted by third parties on such platforms and devices at any time. Information posted may be inaccurate and adverse to us, and it may harm our business or reputation. The harm may be immediate without affording us an opportunity for redress or correction. Further, such inaccurate information may require us to engage in a defensive media campaign, which may divert our management's attention or result in an increase in our